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(54) IMIDAZO[4,5-b]PYRIDINES

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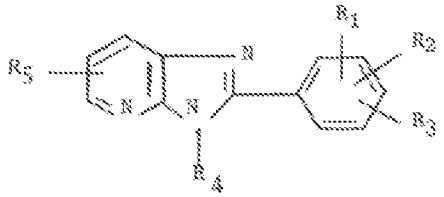
ABSTRACT OF THE DISCLOSURE

This invention relates to new imidazo[4,5-b]pyridine having valuable physiological properties, in particular an activity on the blood pressure and heart force, a positive inotropic effect, an antiulcus activity, a platelet aggregation inhibiting effect and a prolonging activity on the bleeding time. Tests on certain of the new compounds with regard to their physiological properties are described. Processes for the preparation of the new compounds are described and exemplified and examples of pharmaceutical compositions containing the new compounds are given.

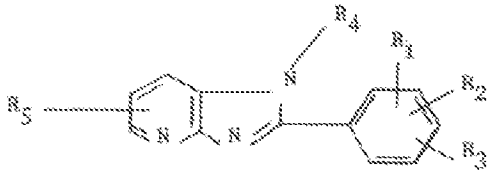
The present invention relates to new imidazo [4,5-b]pyridines having interesting physiological properties.

According to one feature of the present invention there are provided compounds of general formula:



(I)

and isomers thereof of general formula:



(Ia)

wherein R_1 represents an alkylamino, dialkylamino, hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group, or an alkoxy group optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, 4-alkylpiperazino, 4-phenyl-piperazino, 4-methoxyphenylpiperazino, 4-phenylethylpiperazino, phenyl-ethylamino, N-methyl-phenylethylamino or N-methyl-dimethoxy-phenylethyl-amino group;

R_2 represents a hydrogen or halogen atom or a hydroxy, methoxy, ethoxy, methyl, methylthio, methylsulfinyl or methylsulfonyl group;

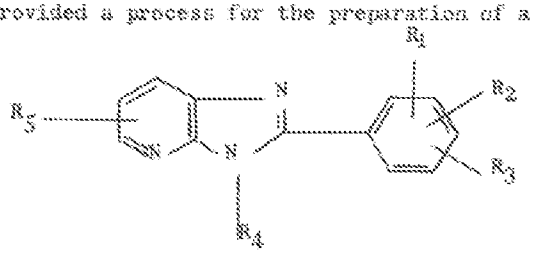
R_3 represents a hydrogen atom or a methoxy group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the remaining R_1, R_2 or R_3 group is as hereinbefore defined;

R_4 represents a hydrogen atom, an alkyl group optionally substituted by a hydroxy, phenyl, dimethoxyphenyl, dialkylamino, piperidino, morpholino, 4-methylpiperazino or 4-phenylpiperazino group, or a phenyl

group optionally substituted by a halogen atom or by one or two methoxy groups, whereby each of the above mentioned alkyl or alkoxy groups contain from 1 to 4 carbon atoms; and

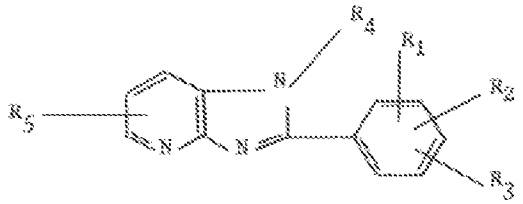
R_5 represents a hydrogen atom, a halogen atom or a lower alkyl group and the corresponding imidazo [4,5-b] pyridine-N-oxides and isomers thereof and acid addition salts thereof.

According to another feature of the invention, there is also provided a process for the preparation of a compound of the general formula:



(I)

or an isomer thereof of the general formula:



(Ia)

wherein R_1 represents an alkylamino, dialkylamino, hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group, or an alkoxy group optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, 4-alkylpiperazino, 4-phenyl-piperazino, 4-methoxyphenylpiperazino, 4-phenylethylpiperazino, phenyl-ethylamino, N-methyl-phenylethylamino or N-methyl-dimethoxy-phenylethyl-amino group;

R_2 represents a hydrogen or halogen atom or a hydroxy, methoxy, ethoxy, methyl, methylthio, methylsulfinyl or methylsulfonyl group;

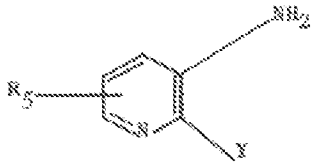
R_3 represents a hydrogen atom or a methoxy group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the

remaining R_1, R_2 or R_3 group is as hereinbefore defined;

R_4 represents a hydrogen atom, an alkyl group optionally substituted by a hydroxy, phenyl, dimethoxyphenyl, dialkylamino, piperidino, morpholino, 4-methylpiperazino or 4-phenylpiperazino group, or a phenyl group optionally substituted by a halogen atom or by one or two methoxy groups, whereby each of the above mentioned alkyl or alkoxy groups contain from 1 to 4 carbon atoms; and

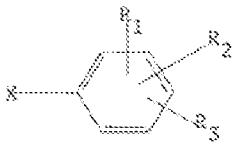
R_5 represents a hydrogen atom, a halogen atom or a lower alkyl group and the corresponding imidazo [4,5b] pyridine-N-oxides and isomers thereof and pharmaceutically acceptable acid addition salts thereof, which comprises, either: -

(a) reacting a compound of the formula:



(II)

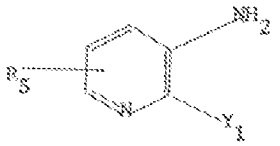
wherein R_5 is as hereinbefore defined and Y represents a group of the formula R_4NH-, wherein R_4 is as hereinbefore defined, with a compound of the formula



(III)

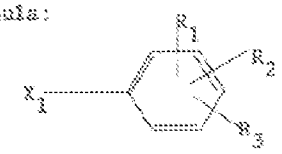
wherein R_1, R_2 and R_3 are as hereinbefore defined and X represents a carboxyl, thiocarboxyl or dithiocarboxyl group, or functional derivative thereof; or

(b) reacting a compound of the formula:



(IIa)

wherein R_5 is as hereinbefore defined and Y represents a halogen atom, with a compound of the formula:



(IIIa)

wherein R_1, R_2 and R_3 are as hereinbefore defined and X_1 represents an appropriate $-NR_4$ containing group which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group; and when a pharmaceutically acceptable acid addition salt is required converting a base of formula I obtained into such a salt.

In general the compounds of general formula I and isomers thereof of general formula Ia possess valuable physiological properties, in particular an activity on the blood pressure and heart force, a positive isotropic effect, an antiulcus activity, a platelet aggregation inhibiting effect and a prolonging activity on the bleeding time.

B

Preferred compounds according to the invention by virtue of their particularly favourable physiological properties are those(wherein R_1, R_4 and R_5 represent hydrogen atoms and R_2 and R_3, which may be the same or different, each represents a halogen atom or a methyl, methoxy, ethoxy, alkylthio, alkylsulfinyl, dialkylamino-alkoxy, morpholinoalkoxy, thiomorpholinoalkoxy, 4-methylpiperazinoalkoxy, 4-phenylpiperazinoalkoxy or alkylsulfinylalkoxy group (wherein each alkyl group contains from 1 to 3 carbon atoms and each alkoxy group contains 2 or 3 carbon atoms)and physiologically compatible acid addition salts thereof. Particularly preferred are the following compounds:-

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine and physiologically compatible acid addition salts thereof,

2-(2-Methoxy-4-methylmercapto-phenyl)-1H-imidazo-[4,5-b] pyridine and physiologically compatible acid addition salts thereof,

2-(2-Methoxy-4-methylsulfinyl-phenyl)1H-imidazo [4,5-b] pyridine and physiologically compatible acid addition salts thereof,

2-(2-Methoxy-4-methyl-phenyl)-1H-imidazo[4,5-b] pyridine and physiologically compatible acid addition

salts thereof,

2-(2-Methoxy-5-methylmercapto-phenyl)-1H-imidazo [4,5-b] pyridine and physiologically compatible acid addition salts thereof, and

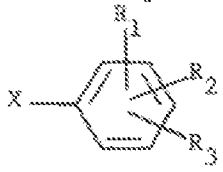
2-(2-Ethoxy-4-methyl-phenyl)-1H-imidazo[4,5-b] pyridine and physiologically compatible acid addition salts thereof.

The new compounds of general formula I and isomers thereof of general formula Ia as hereinbefore defined may be prepared by either of the following processes, which processes constitute further features of the invention:-

a) Reaction of a compound of formula

(II)

[wherein R_5 is as hereinbefore defined and Y represents a group of formula R_4NH-(wherein R_4 is as hereinbefore defined)] with a compound of formula

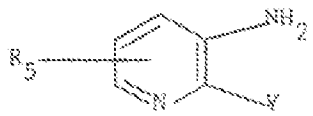


(III)

(wherein R_1 to R_3 are as hereinbefore defined and X represents a carboxyl, thiocarboxyl or dithiocarboxyl

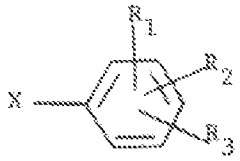
group) or a functional derivative thereof, for example an acid halide, anhydride, ester or orthoester; and

b) Reaction of a compound of formula



(II)

(wherein R_5 is as hereinbefore defined and Y represents a halogen atom) with a compound of formula



(III)

[wherein R_1 to R_3 are as hereinbefore defined and X represents an appropriate $-NR_4$ containing group (wherein R_4 is as hereinbefore defined) which is derived from a carboxyl, thicarboxyl or dithiocarboxyl group, for example a nitrile, amide, amido ester, imido thioester, imido halide or amidine group].

In each case the reaction is preferably carried out in the presence of a solvent, suitable solvents including for example benzene, pyridine, glycol, toluene, acetone, diethylene glycol and triethylamine. However the reaction may also be performed in the absence of a solvent

The reaction temperature used is determined by the reactivity of the group X in the compound of formula III used but generally the reaction is effected at temperatures from -20 to 250°C. If desired the reaction may be effected in the presence of an acid binding agent, such as pyridine or triethylamine, or in the presence of a catalytic quantity of an acid, such as p-toluenesulfonic acid, or in the presence of a dehydrating agent,such as phosphorus oxychloride or thionyl chloride.

If for example a compound of formula III wherein X represents a carboxyl or amide group is used the reaction if conveniently carried out in the presence of phosphorus oxychloride or thionyl chloride, if desired in the presence of a tertiary organic base such as pyridine or triethylamine, preferably at temperatures from -20°C up to the boiling point of the solvent used, e.g. at 120°C.

If for example a compound of formula III wherein X represents a nitrile group is used, the reaction is conveniently performed in the presence of a catalytic quantity of an acid, such as p-toluenesulfonic acid, preferably at temperatures from 120 to 180°C, e.g. at 160°C, optionally in the presence of a solvent.

If for example a compound of formula III wherein X represents a thioamide group is used, the reaction is conveniently effected in the presence of a solvent, such as glycol, and preferably at temperatures from 100 to 150°C, e.g at 130°C.

If a compound of formula II wherein Y represents a halogen atom, e.g. a chlorine atom is used, the reaction is preferably carried out via the corresponding amidine, which is cyclized at elevated temperatures, e.g. at temperatures from 100 to 200°C, optionally without previous isolation.

The compounds of general formula I and isomers thereof of general formula Ia containing a reactive halogen atom obtained according to the processes of the present invention may, if desired, be subsequently converted into the corresponding amino compounds with amines, and/or compounds of general formula I and isomers thereof of general formula Ia containing reactive hydrogen atoms, may if desired be subsequently alkylated by means of an alkylating agent in the presence of a base.

In addition a compound of formula I or an isomer thereof of formula Ia may if desired be converted into the

corresponding N-oxide, S-oxide or S,S-oxide compound by means of an oxidizing agent. Finally a compound of formula I or an isomer thereof of formula Ia may if desired be converted into an acid addition salt thereof, preferably into a physiologically compatible acid addition salt. Suitable acids include for example hydrochloric acid, hydrobromic acid, sulfuric acid, lactic acid, citric acid, tartaric acid, maleic acid and fumaric acid.

The starting compounds used for the processes according to the invention are known from the literature, or they may be prepared according to known processes (see Examples).

As already mentioned above, the new compounds of general formula I and isomers thereof of general formula Ia in general show valuable pharmacological properties, those which have been tested showing especially an activity on the blood-pressure, a positive inotropic activity, an antiulcus activity, a platlet aggregation inhibiting effect and a prolonging activity on the bleeding time.

The following compounds have been tested with respect to certain of their biological activities:

A = 2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride,

B = 2-[2-(2-Methylsulfinyl-ethoxy)-4-methoxy-phenyl]-1H-imidazo-[4,5-b]pyridine hydrochloride,

C = 2-(2-Methoxy-4-methylmercapto-phenyl)-1H-imidazo [4,5-b]pyridine hydrochloride

D = 2-(2-Methoxy-4-methylsulfinyl-phenyl)-1H-imidazo [4,5-b]pyridine hydrochloride,

E = 2-(2-Methoxy-5-methylmercapto-phenyl)-1H-imidazo [4,5-b]pyridine hyrochloride

F = 2-(2-Methoxy-4-methyl-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

G = 2-(2-Ethoxy-4-methoxy-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride,

H = 2-(2-Ethoxy-4-methyl-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride,

I = 2-(2-Methoxy-4-chloro-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride and

J = 2-[2-(2-Methylsulfinyl-ethoxy)-4-methylmercapto-phenyl]-1H-imidazo[4,5-b]pyridine hydrochloride

1. Positive inotropic activity in the isolated auricle of the guinea-pig:

Isolated auricles of guinea-pigs were put into an organ bath of 100 ml. The bath has been filled with a tyrode solution

at a temperature of 30°C. The tyrode solution was infused with carbogen (95% of O_2 and 5% of CO_2). The spontaneous contractions of the auricles were registered isometrically with a Statham-Force-transducer on a Grass-polygraph. The auricles were charged with 1 g. After sufficient equilibrating time, the substances in question were added to the organ bath. The concentration of the substance in the bath was 1×10^{-5} g/ml in each case. 5 auricles were used for each solution.

The following Table gives the results:

Table I

Substance	Increase of the contraction-amplitude in %
A	57.0
B	17.5
C	10.3
E	40.9
F	50.2
G	33.9
H	42.9
I	21.4
J	11.4

2. Circulation experiments on the narcotized cat:

Cat were narcotized with 30 mg/kg of pentobarbital-sodium i.v. A plastic catheter was introduced into the arteria femoralis and into the left ventricle of the heart a steel catheter was introduced from the arteria carotis. With Statham-pressure-transducers of the type P23 AA and P23 Dc, the arterial blood-pressure and the pressure in the left ventricle was registered continuously. From the ventricle-pressure-curve, the contractility parameters dp/dt_{max} and V_{CE} were continuously determined by means of an analogous computer. The heart frequency was ascertained from the ventricle-pressure-curve using a tachograph. In addition, the EKG was registered in the II derivation.

All registrations were effected on a Brush-direct-writer. The substances were injected over a vena cannula into the vena femoralis. At least three cats were used for the test on each substance.

The following Table gives the results:

Table II

Substance	Dose mg/kg i.v.	Blood-pressure alteration in mm Hg	Heart activity: Alteration of the contraction force in %	Heart activity: Alteration of the heart frequency in %
A	0,5	- 5	+ 20	+ 4
	1,0	- 5	+ 41	+ 5
B	0,5	+ 10	+ 16	- 2
	1,0	+ 20	+ 29	- 9
C	0,5	+ 5	+ 22	+ 1
	1,0	+ 10	+ 36	+ 5
D	0,5	0	+ 34	+ 5
	1,0	- 5	+ 39	+ 5
E	0,5	+ 10	+ 14	0
	1,0	+ 15	+ 25	0
F	0,5	+ 10	+ 44	- 3
	1,0	+ 15	+ 53	0
G	0,5	0	+ 7	0
	1,0	+ 5	+ 29	- 5
H	0,5	+ 10	+ 15	0
	1,0	+ 15	+ 25	0
I	0,5	- 5	+ 17	+ 2
	1,0	- 5	+ 19	+ 2
J	0,5	+ 10	+ 14	0
	1,0	+ 15	+ 22	- 15

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None of the compounds showed any toxic side effects using the doses applied.

According to yet a further feature of the present invention there are provided pharmaceutical compositions comprising as active ingredient at least one compound of formula I or isomer thereof of formula Ia or physiologically compatible acid addition salt thereof in association with a pharmaceutical carrier or excipient.

The compositions may for example be presented in a form suitable for oral, rectal or parenteral administration. Thus for example compositions for oral administration may be solid or liquid and may take the form of tablets, coated tablets or drops, such compositions comprising carriers or excipients conventionally used in the pharmaceutical art.

For parenteral administration the carrier may be a parenterally acceptable liquid, such as sterile water or a parenterally acceptable oil, e.g. arachis oil, contained in ampoules. For rectal administration compositions may take the form of suppositories, the carrier comprising a suppository base.

Advantageously the compositions may be formulated as dosage units. Each dosage unit preferably contains from 35 to 200 mg, preferably from 50 to 100 mg, of active ingredient.

The following Examples serve to illustrate the preparation of compounds according to the invention and of pharmaceutical compositions containing the same.

Example 1

2-(2,4-Dimethoxyphenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

54.5 g of 2,3-diaminopyridine and 91.1 g of 2,4-dimethoxybenzoic acid were finely pulverized and added in small amounts to 1500 ml of phosphorus oxychloride whilst stirring. Afterwards, the mixture was refluxed for 2 hours, and the phosphorus oxychloride was distilled off in vacuo. The residue was triturated with 2000 ml of 2N hydrochloric acid and the solid product obtained was suction filtered and recrystallized from water.

Yield: 121 g (65% of theory), m.p.: 238°C

Example 2

2-(2,4-Dimethoxyphenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

360 mg of 2,4-dimethoxybenzoic acid were dissolved in 2 ml of pyridine and a solution of 220 mg of 2,3-diaminopyridine in 2 ml of pyridine was added, whereupon the corresponding salt precipitated out. Whilst

stirring and ice-cooling, 0.38 ml of phosphorus oxychloride were added dropwise and the mixture was stirred for a further hour at 0°C and 1 hour at room temperature. Subsequently the excess of pyridine was removed in vacuo and the residue was dissolved by adding dilute hydrochloric acid. The mixture was neutralised with sodium hydroxide solution and extracted with ethyl acetate. The ethyl acetate layer was evaporated, the residue was treated with a small quantity of 2N hydrochloric acid, and the precipitate was suction filtered and recrystallized from water.

M.p.: 238 to 239°C.

Example 3

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 2 from 2,3-diaminopyridine, 2,4-dimethoxybenzoic acid and thionyl chloride.

M.p.: 238 to 239°C.

Example 4

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

900 mg of 2,4-dimethoxy-benzoic acid were converted into the acid chloride by heating in a mixture of 3 ml of benzene and 2 ml of thionyl chloride. Subsequently, the mixture was evaporated in vacuo and the residue obtained was taken up in 5 ml of benzene. This solution was dropped into a solution of 550 mg of 2,3-diamino-pyridine in 5 ml of pyridine whilst stirring. Afterwards, the mixture was heated for a short time at 60°C, then cooled to room temperature, and 0.9 ml of phosphorus oxychloride were added dropwise. After the mixture had been stirred for a further 3 hours at room temperature, 2N hydrochloric acid was added. The mixture was then neutrallized and extracted with ethyl acetate. The ethyl acetate layers were evaporated and a small quantity of 2N hydrochloric acid was added to the residue. The crystals which precipitated were suction filtered and recrystallized

from water.

M.p.: 237 to 238°C.

Example 5

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

a) 2-Amino-3-(2,4-dimethoxybenzoyl-amino)-pyridine hydrochloride

530 mg of 2,4-dimethoxybenzoic acid were converted into the acid chloride analogously to Example 4 and this acid chloride was dissolved in 1 ml of benzene. The solution obtained was added dropwise to a mixture of 440 mg of 2,3-diamino-pyridine, 3 ml of pyridine and 2 ml of triethylamine. After the whole mixture had been stirred for a further 2 hours at room temperature, water was added, the mixture was neutralized with concentrated hydrochloric acid and extracted with ethyl acetate. The ethyl acetate was removed, the residue was treated with dilute hydrochloric acid, the precipitated crystals were suction filtered and recrystallized from ethanol.

M.p.: 172 to 174°C.

b) 2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

155 mg of 2-amino-3-(2,4-dimethoxybenzoyl-amino)-pyridine hydrochloride were dissolved in 2 ml of pyridine. 0.2 ml of phosphorus oxychloride were dropped in whilst stirring at room temperature. After 2 hours the mixture was poured into water and worked up analogously to Example 4.

M.p.: 237 to 238°C.

Example 6

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

155 mg of 2-amino-3-(2,4-dimethoxybenzoyl-amino)-pyridine hydrochloride were heated for 5 minutes at 200 - 210°C. The mixture was treated with a small quantity of 2N hydrochloric acid, and the precipitate was filtered and recrystallized from water.

M.p.: 237 to 238°C.

Example 7

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

155 mg of 2-amino-3-(2,4-dimethoxybenzoyl-amino)-pyridine hydrochloride were refluxed for 30 minutes in 2 ml of glycol. The mixture was then diluted with water, neutralized, extracted with ethyl acetate and processed analogously to Example 4.

M.p.: 238 to 239°C.

Example 8

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

5.45 g of 2,3-diaminopyridine were added in small amounts to 150 ml of phosphorus oxychloride whilst stirring and 9.81 g of methyl 2,4-dimethoxybenzoate were also added dropwise. The mixture was then heated at 120°C. After two hours the excess of phosphorus oxychloride was evaporated in vacuo, the residue was digested with 2N hydrochloric acid and the solid product obtained was suction filtered and recrystallized from water.

M.p.: 238 to 239°C.

Example 9

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

0.5 ml of morpholine were added whilst stirring to 470 mg of 2,4-dimethoxybenzoyl chloride in 6 ml of toluene. After 20 minutes the toluene was evaporated, the residue was treated with dilute hydrochloric acid and this mixture was extracted with ethyl acetate. After washing the ethyl acetate layer with sodium bicarbonate solution and evaporating off the solvent, crude 2,4-dimethoxybenzoyl-morpholine was obtained as oil. This oil was dissolved in 5 ml of pyridine, 250 mg of 2,3-diaminopyridine was added and finally 1 ml of phosphorus oxychloride was added dropwise whilst stirring and ice-cooling. After stirring for 5 hours at 0°C, ice-water was added, the mixture was made alkaline with concentrated ammonia, heated for a short time on the steam bath and extracted with ethyl acetate. The ethyl acetate was removed, and the residue obtained was treated with 2N hydrochloric acid, suction

filtered and recrystallized from water.

M.p.: 238°C.

Example 10

2-(2,4-Dimethoxyphenyl)-1H-imidazo(4,5-b)pyridine hydrochloride

300 mg of 2,4-dimethoxybenzoyl-(4-chloro-anilide) and 110 mg of 2,3-diaminopyridine were mixed and added in small amounts to 3 ml of phosphorus oxychloride whilst stirring. Afterwards the mixture was refluxed for 8 hours. Then the phosphorus oxychloride was removed in vacuo, the residue was triturated with 2N hydrochloric acid and the solid product obtained was suction filtered and recrystallized from water.

M.p.: 237 to 238°C.

Example 11

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

600 mg of 2,4-dimethoxybenzoyl-(4-chloro-anilide) in a mixture of 5 ml of benzene and 2 ml of thionyl

chloride were refluxed for 3 hours. After the mixture had been evaporated the crude 2,4-dimethyl-N-(4-chlorophenyl)-benzimidic acid chloride was obtained as an oil. This oil was dissolved in 9 ml of toluene and the solution was added to a solution of 200 mg of 2,3-diaminopyridine in 10 ml of isopropanol. The mixture was heated for 10 minutes at 70°C. The 2,4-dimethoxy-benzoic acid-N-(4-chlorophenyl)-N'-(2-amino-3-pyridyl)-amidine hydrochloride which formed was not isolated but was dissolved in 20 ml of glycol after removing the isopropanol in vacuo. The glycol solution was refluxed for 10 minutes. Subsequently water was added, the mixture was made alkaline with concentrated ammonia, extracted with ethyl acetate and worked up as described in Example 4. M.p.: 237 to 238°C.

Example 12

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

100 mg of 2,3-diaminopyridine, 200 mg of 2,4-dimethoxybenzonitrile and 400 mg of p-toluenesulfonic acid

monohydrate were mixed together and heated for 3½ hours at 160°C. The product was triturated with dilute ammonia and ethyl acetate until the whole product had dissolved. The aqueous layer was extracted with ethyl acetate. After some time, when the combined ethyl acetate layers had been extracted with a small quantity of 2N hydrochloric acid, the product crystallized out from the aqueous phase.

M.p.: 237 to 238°C.

Example 13

2-(3,4,5-Trimethoxyphenyl)-1H-imidazo[4,5-b]pyridine

3.4 g of p-toluenesulfonic acid monohydrate and 15 ml of benzene were heated at 120°C until all the benzene had evaporated. Subsequently 1.1 g of 2,3-diaminopyridine and 2 g of 3,4,5-trimethoxybenzoyl nitrile were added and the mixture was heated for 2 hours at 150°C. After cooling, water was added, the mixture was extracted with ethyl acetate, the ethyl acetate layers were washed with dilute sodium hydroxide solution, evaporated and the residue was recrystallized from isopropanol/petroleum

ether.

M.p.: 226°C.

Example 14

2-(3,4,5-Trimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine

A mixture of 4.2 g of 3,4,5-trimethoxybenzoic acid and 2.2 g of 2,3-diaminopyridine was refluxed for 2 hours in 40 ml of phosphorus oxychloride. Subsequently the excess of phosphorus oxychloride was distilled off, water was added to the residue and the precipitated solid product was suction filtered. The product was dissolved in hot water, made alkaline with concentrated ammonia, and the precipitate was suction filtered and recrystallized from a small quantity of isopropanol.

M.p.: 225 to 226°C.

Example 15

2-(2,5-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine

a) 2,5-Dimethoxy-thiobenzoyl morpholide

A mixture of 10 g of 2,5-dimethoxybenzaldehyde, 10 g of morpholine and 4 g of sulfur was heated at 130°C for 3½ hours and subsequently dissolved in 300 ml of hot ethanol. The product which precipitated out on cooling,

was recrystallized from ethanol.

M.p.: 127°C.

b) S-Methyl-2,5-dimethoxy-thiobenzoyl morpholide iodide

6 g of 2,5-dimethoxy-thiobenzoyl morpholide, 6.5 g of methyl iodide and 30 ml of acetone were refluxed for 8 hours. Subsequently the precipitated solid product was suction filtered and washed with ether. The product obtained was not purified further.

c) 2-(2,5-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine

2 g of S-methyl-2,5-dimethoxy-thiobenzoyl morpholide iodide and 1.1 g of 2,3-diaminopyridine were heated in 30 ml of glycol for 40 minutes at 130°C. Subsequently the mixture was poured on ice-water, suction filtered and recrystallized from ethanol/water.

M.p.: 235°C.

Example 16

2-(4-Hydroxy-phenyl)-1H-imidazo[4,5-b]pyridine

a) 4-Hydroxy-thiobenzoyl morpholide

Prepared analogously to Example 15a from 12.2 g of

4-hydroxy-benzaldehyde, 16 g of morpholine and 3.2 g of sulfur.

M.p.: 205°C

b) S-Methyl-4-hydroxy-thiobenzyl morpholide iodide

Prepared analogously to Example 15b from 14.4 g of 4-hydroxy-thiobenzyl morpholide and 2.1 g of methyl iodide in 100 ml of acetone.

M.p.: 181°C.

c) 2-(4-Hydroxy-phenyl)-1H-imidazo[4,5-b]pyridine

1.84 g of S-methyl-4-hydroxy-thiobenzyl morpholide iodide were heated for 20 minutes at 130°C with 1.1 g of 2,3-diaminopyridine in 30 ml of glycol. The product precipitated whilst cooling and was dissolved in sodium hydroxide solution and reprecipitated with an acid.

Analysis:	Calculated:	65.87% C	5.13% H	16.46% N
	Found:	65.90% C	5.16% H	16.47% N

Example 17

2-[4-Methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

a) 4-Methoxy-2-(3-chloro-propoxy)-benzoyl morpholide

21.9 g of 2-hydroxy-4-methoxy-benzoyl morpholide were dissolved in 200 ml of dimethylformamide and 11.2 g of potassium tert.-butoxide were added. After the whole product had dissolved, 50 g of 1-chloro-3-bromopropane were added and the mixture was heated for 2 hours at 130°C. Subsequently the mixture was evaporated in vacuo, the residue was dissolved in ethyl acetate, and the solution was washed with sodium hydroxide solution and water and evaporated.

b) 2-[4-Methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

20 g of 4-methoxy-2-(3-chloro-propoxy)-benzoyl morpholide, 7 g of 2,3-diamino-pyridine and 170 ml of phosphorus oxychloride were refluxed for 2 hours. After

evaporation of the phosphorus oxychloride, the residue was mixed with water, neutralized with sodium hydroxide solution and extracted with ethyl acetate. The hydrochloride was precipitated with ethereal hydrochloric acid.

M.p.: 198°C (decomp).

Example 18

2-[4-Methoxy-2-(2-chloroethoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

a) 4-Methoxy-2-(2-hydroxy-ethoxy)-benzoyl morpholide

23.7 g of 2-hydroxy-4-methoxy-benzoyl morpholide, 33.6 g of potassium tert.-butoxide and 37.4 g of ethylene bromohydrin were heated in 100 ml of dimethylformamide for 6 hours at 120°C. After evaporation in vacuo, the residue was dissolved in chloroform and the solution was washed with sodium hydroxide solution and water and evaporated.

b) 2-[4-Methoxy-2-(2-chloroethoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

2.8 g of 4-methoxy-2-(2-hydroxy-ethoxy)-benzoyl morpholide, 1.1 g of 2,3-diaminopyridine and 20 ml of phosphorus oxychloride were refluxed for 2 hours. After

evaporation water was added, the mixture was neutralized, extracted with ethyl acetate and the hydrochloride was precipitated with ethereal hydrochloric acid from the organic layer.

M.p.: 110°C (decomp.).

Example 19

2-[4-Methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

a) 4-Methoxy-2-(3-chloropropoxy)-benzoyl anilide

2.3 g of 2-hydroxy-4-methoxy-benzoyl anilide, 5 ml of 1-chloro-3-bromopropane, 1.12 g of potassium tert.-butoxide and 20 ml of dimethylformamide were heated for 2 hours at 130°C. Subsequently the mixture was evaporated in vacuo, water was added and the mixture was suction filtered.

M.p.: 87 to 90°C.

b) 2-[4-Methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

Prepared analogously to Example 17b from 4-methoxy-

2-(3-chloropropoxy)-benzoyl anilide and 2,3-diamino-pyridine.

M.p.: 198°C.

Example 20

2-[4-Methoxy-2-(3-morpholino-propoxy)-phenyl]-1H-imidazo [4,5-b]-pyridine

0.5 g of 2-[4-methoxy-2-(3-chloroproxy)-phenyl]-1H-imidazo[4,5-b]-pyridine hydrochloride were refluxed for 4½ hours in 5 ml of morpholine. Water was then added, the precipitate was suction filtered and recrystallized from water.

M.p.: 108 to 110°C.

Example 21

2-[4-Methoxy-2-(2-(4-phenyl-1-piperazinyl)-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared from 1.7 g of 2-[4-methoxy-2-(2-chloro-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine and 3.2 g of 1-phenylpiperazine by boiling for 8 hours in ethanol.

M.p.: 164 to 165°C (from isopropanol)

Example 22

2-[4-Methoxy-2-(3-dimethylamino-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine . hydrochloride

1.8 g of 2-[4-methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine hydrochloride and 20 ml of saturated dimethylamine solution in ethanol were heated for 8 hours in a closed vessel at 100°C. Subsequently the mixture was evaporated in vacuo and recrystallized from isopropanol.

M.p.: 209 - 210°C

Example 23

2-[4-Methoxy-2-(3-dimethylamino-propoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine dihydrochloride

1.64 g of 4-methoxy-2-(3-dimethylamino-propoxy)-thiobenzoyl morpholide were dissolved in a mixture of 17 ml of glacial acetic acid and 3 ml of acetic anhydride. 1 ml of dimethyl sulfate was added and the mixture was heated on the steam bath for 1 hour. Subsequently, the mixture was evaporated in vacuo. The crude S-methyl-4-methoxy-2-(3-dimethylamino-propoxy)-thiobenzoyl morpholide methyl

sulfate obtained was dissolved in 13 ml of glycol 0.7 g of 2,3-diaminopyridine was added and the mixture was heated for 2 hours at 160°C. Subsequently, the mixture was poured into 50 ml of water, 5 ml of concentrated ammonia were added and the mixture was extracted with ethyl acetate. The ethyl acetate layers were evaporated, the residue was dissolved in ethanol, ethereal hydrochloric acid was added and it was again evaporated. The residue crystallized after trituration with toluene and a small quantity of ethanol. The product was suction filtered and recrystallized from isopropanol.

M.p.: of the dihydrochloride hydrate: 228 to 235°C (decomp.).

Example 24

2-(2,4-Dimethoxy-phenyl)-3-methyl-3H-imidazo[4,5-b] pyridine

800 mg of 2,4-dimethoxybenzoyl methylamide were refluxed for 3 hours with 500 mg of 2-chloro-3-aminopyridine in 10 ml of phosphorus oxychloride. Subsequently, the

mixture was poured into water, neutralized with concentrated ammonia and extracted with ethyl acetate. After evaporation, the crude N-methyl-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine obtained was dissolved in 10 ml of 10% glycolic sodium hydroxide solution and heated for 4 hours at 180 to 190°C. The mixture was poured into water and extracted with ethyl acetate. The compound obtained was purified by column chromatography (silica gel, eluent $CHCl_3$: MeOH = 19 : 1).

M.p. of the hydrochloride: 196 to 197°C

Example 25

2-(2,4-Dimethoxy-phenyl)-3-(4-chlorophenyl)-1H-imidazo [4,5-b] pyridine

3 g of 2,4-dimethoxy-benzoyl (4-chloroanilide) and 1.3 g of 2-chloro-3-aminopyridine were refluxed for 2 hours in 16 ml of phosphorus oxychloride. Subsequently the mixture was poured into water, neutralized with concentrated ammonia and extracted with ethyl acetate. The ethyl acetate layer was extracted with 3N hydrochloric acid.

After neutralization of the aqueous layer, the mixture was again extracted with ethyl acetate. The solid product remaining after evaporation of the organic layer was recrystallized from methanol.

M.p.: 176 to 178°C.

Example 26

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

2.2 g of 2,3-diaminopyridine, 6.8 g of the imide chloride of 2,4-dimethoxy-benzoyl morpholide and 12 ml of triethylamine were heated for ½ hour at 120°C in 10 ml of diethyleneglycol dimethyl ether. After cooling, water was added, the reaction mixture was extracted with chloroform and the chloroform layer was extracted with 2N sodium hydroxide solution. The yellow hydrochloride which precipitated from the acidic solution was converted into the base with ammonia, and was purified by column chromatography. The hydrochloride was again precipitated from acetone with ethereal hydrochloric acid.

M.p.: 237 to 238°C.

Example 27

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared from 1.1 g of 2,3-diaminopyridine and 3.5 g of 2,4-dimethoxybenzoyl anhydride by heating for 5 hours at 180°C. The further processing was carried out as in Example 26.

M.p.: 236 to 238°C.

(A)

Example 28

2-(2-Methoxyphenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

a) 2-Methoxy-thio-benzoic acid-morpholide

34 g of 2-methoxybenzaldehyde, 16 g of sulfur and 32,6 g of morpholine were heated for 3 hours up to 120°C. The reaction mixture thus obtained was taken up in ethanol, filtered, cooled and the precipitated yellow crystals were suction filtered.

Yield: 54,1 g (91 % of theory), m.p.: 80 to 82°C.

b) 2-Methoxy-thio-benzoic acid-morpholide-methoiddide

47,4 g of 2-methoxy-benzoic acid-thiomorpholide were refluxed for 1 hour in 150 ml of acetone with 25 ml of methyl iodide and the precipitated yellow crystals were suction filtered after cooling.

Yield: 64,4 g (85 % of theory), m.p.: 162 to 164°C.

c) 2-(2-Methoxyphenyl)-1H-imidazo[4,5-b]pyridine

19 g of 2-methoxy-thio-benzoic acid-morpholide-methoidide and 8,7 g of 2,3-diaminopyridine were heated for 3 hours at 120°C in 70 ml of glycol. After cooling, water was added, the mixture was made alkaline with ammonia and extracted with chloroform. The organic layer was washed with water and subsequently 2n hydrochloric acid was added. The precipitated product was suction filtered, the base was set free with ammonia, taken up in chloroform and purified over a silica gel column. The colorless hydrochloride was obtained from acetone by addition of ethereal hydrochloric acid.

M.p.: 233 to 234°C.

Example 29

2-(2-Methoxyphenyl)-3-methyl-3H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2-methylamino-3-amino-pyridine and 2-methoxy-thio-benzoic acid-morpholide-methiodide.

M.p.: 208 to 210°C.

Example 30

2-[2-(2-Methoxy-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2-(2-methoxy-ethoxy)-thio-benzoic acid-morpholide-methiodide and 2,3-diaminopyridine.

M.p.: 170 to 172°C.

Example 31

2-(4-Methoxyphenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 4-methoxy-thio-benzoic acid-morpholide-methiodide (m.p.: 142 to 144°C) and 2,3-diamino-pyridine.

M.p.: 243 to 245°C.

Example 32

2-(3-Methoxy-4-hydroxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 3-methoxy-4-hydroxy-thio-benzoic acid-morpholide-methiodide (m.p.: 178 to 180°C) and 2,3-diaminopyridine.

M.p.: 251 to 254°C.

A

Example 33

2-(2,3-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2,3-dimethoxy-thio-benzoic acid-morpholide-methoiodide (m.p.: 138 to 140°C) and 2,3-diamino-pyridine.

M.p.: 270 to 272°C.

Example 34

2-(2-Hydroxy-4-methoxy-phenyl)-1H-imidazo[4,5,-b]pyridine-hydro-chloride

Prepared analogous to example 28 from 2-hydroxy-4-methoxy-thio-benzoic acid-morpholide-methoiodide (m.p.: 180 to 181°C) and 2,3-diaminopyridine.

M.p.: 190 to 192°C (decomp.).

M.p. of the free base: 292 to 293°C.

Example 35

2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2,4-dimethoxy-thio-benzoic acid-morpholide-methoiodide (m.p.: 138 to 140°C (decomp.)) and 2,3-diaminopyridine.

M.p.: 238°C (from methanol)

A

Example 36

2-(2,4-Dimethoxy-phenyl)-6-methyl-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 35 from 2,3-diamino-5-methyl-pyridine and 2,4-dimethoxy-thio-benzoic acid-morpholide-metholodide.

M.p.: 260 to 261°C.

Example 37

2-(2,4-Dimethoxy-phenyl)-7-methyl-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 35 from 2,3-diamino-4-methyl-pyridine and 2,4-dimethoxy-thio-benzoic acid-morpholide-metholodide.

M.p.: 230 to 231°C.

Example 38

2-(2,4-Dimethoxy-phenyl)-5-methyl-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 35 from 2,3-diamino-6-methyl-pyridine and 2,4-dimethoxy-thio-benzoic acid-morpholide-metholodide.

M.p.: 245 to 246°C.

Example 39

2-(2,4-Dimethoxy-phenyl)-6-chloro-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 35 from 2,3-diamino-5-chloro-pyridine

A

and 2,4-dimethoxy-thio-benzoic acid-morpholide-methoiodide.

M.p.: 253 to 255°C.

Example 40

2-(2-Ethoxy-4-methoxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2-ethoxy-4-methoxy-thio-benzoic acid-morpholide-methoiodide (m.p.: 152 to 154°C) and 2,3-diamino-pyridine.

M.p.: 228 to 230°C.

Example 41

2-(2-Methoxy-4-ethoxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydro-chloride

Prepared analogous to example 28 from 2-methoxy-4-ethoxy-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 224 to 225°C (from methanol)

Example 42

2-(2,4-Diethoxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2,4-diethoxy-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 224 to 226°C.

Example 43

2-[2-(2-Hydroxy-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]-pyridine-hydrochloride

Prepared analogous to example 28 from 2-(2-hydroxy-ethoxy)-4-methoxy-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 237 to 239°C.

Example 44

2-[2-(3-Hydroxy-propoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]-pyridine-hydrochloride

Prepared analogous to example 28 from 2-(3-hydroxy-propoxy)-4-methoxy-thio-benzoic acid-morpholide-methoiodide and 2,3-diamino-pyridine.

M.p.: 170°C (whilst sintering)

Example 45

2-[2-(2-Methoxy-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]-pyridine-hydrochloride

Prepared analogous to example 28 from 2-(2-methoxy-ethoxy)-4-methoxy-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 191 to 193°C.

Example 46

2-[2-Methoxy-4-(2-methylmercapto-ethoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine-hydrochloride

a) 4-(2-Methylmercapto-ethoxy)-2-hydroxy-benzaldehyde

12 g of 2,4-dihydroxy-benzaldehyde and 9,6 g of potassium-tert.-butoxide were dissolved in 80 ml of ethyleneglycolmonomethylether, 9,6 g of methylmercaptoethylchloride were added and the reaction mixture was stirred for 8 hours at 80°C (bath temperature). After removing the solvent, the residue was taken up in diluted sodium hydroxide solution, the mixture was extracted twice with chloroform, the aqueous alkaline solution was separated, acidified and extracted with chloroform. The organic phase was dried and evaporated. The residue was purified by column chromatography (silica gel). The oil thus obtained was processed directly.

b) 4-(2-Methylmercapto-ethoxy)-2-methoxy-benzaldehyde

9,7 g of 4-(2-methylmercapto-ethoxy)-2-hydroxy-benzaldehyde were dissolved in ethanol together with 6,7 g of potassium-tert.-butoxide, 4,3 ml of dimethyl-sulfate were added and the mixture was refluxed for 3 hours. Then again 1 ml of dimethyl-sulfate was added and the mixture was heated for a further hour. After the ethanol had been distilled off, the residue was taken up in water/chloroform and 2n sodium hydroxide solution was added. The chloroform layer was separated, washed with water, dried and evaporated.

M.p.: 99 to 100°C (from cyclohexane)

c) 4-(2-Methylmercapto-ethoxy)-2-methoxy-thio-benzoic acid-morpholide

Prepared analogous to example 38a from 4-(2-methylmercapto-ethoxy)-2-methoxy-benzaldehyde.

M.p.: 131 to 132°C (from ethanol)

d) 2-[2-Methoxy-4-(2-methylmercapto-ethoxy)-phenyl]-1H-imidazo-[4,5-b]-pyridine-hydrochloride

5,4 g of 4-(2-methylmercapto-ethoxy)-2-methoxy-thio-benzoic acid-

morpholide were refluxed for 1 1/2 hours together with 1,2 ml of methyliodide in 50 ml of acetone. After cooling, the solvent was removed and the obtained sirupy methoiodide was heated with 3,6 g of 2,3-diaminopyridine in 20 ml of glycol for 1 1/2 hours up to 120°C. The mixture was diluted with water and extracted with chloroform. Subsequently, 2n hydrochloric acid was added to the organic layer and the yellow precipitate was suction filtered.

M.p.: 197 to 199°C (from methanol)

Example 47

2-/2-Methoxy-4-(2-ethylmercapto-ethoxy)-phenyl/-1H-imidazo/4,5-b/-pyridine-hydrochloride

Prepared analogous to example 46 from 4-(2-ethylmercapto-ethoxy)-2-methoxy-thio-benzoic acid-morpholide and 2,3-diaminopyridine. The purification of the final product was effected by chromatography over silica gel and the precipitation of the hydrochloride was effected by dissolving of the base in acetone and addition of an excess of ethereal hydrochloric acid.

M.p.: 195 to 196°C.

Example 48

2-/2-Methoxy-4-(3-methylmercapto-propoxy)-phenyl/-1H-imidazo-/4,5-b/pyridine-hydrochloride

Prepared analogous to example 46 from 4-(3-methylmercapto-propoxy)-2-methoxy-thio-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 189 to 191°C (decomp.).

Example 49

2-[2-Methoxy-4-(3-ethylmercapto-propoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine-hydrochloride

Prepared analogous to example 46 from 4-(3-ethylmercapto-propoxy)-2-methoxy-thio-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 183 to 185°C (decomp.).

Example 50

2-[2-(2-Methylmercapto-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]-pyridine-hydrochloride

Prepared analogous to example 46 from 2-(2-methylmercapto-ethoxy)-4-methoxy-thio-benzoic acid-morpholide and 2,3-diamino-pyridine.

M.p.: 204 to 206°C (decomp.).

Example 51

2-[2-(2-Ethylmercapto-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]-pyridine-hydrochloride

Prepared analogous to example 46 from 2-(2-ethylmercapto-ethoxy)-4-methoxy-thio-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 193 to 195°C.

Example 52

2-[2-(3-Methylmercapto-propoxy)-4-methoxy-phenyl]-1H-imidazo-[4,5-b]pyridine-hydrochloride

Prepared analogous to example 46 from 2-(3-methylmercapto-propoxy)-4-methoxy-thio-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 191 to 193°C.

[A]

Example 53

2-/2-(3-Ethylmercapto-propoxy)-4-methoxy-phenyl/-1H-imidazo-/4,5-b/pyridine-hydrochloride

Prepared analogous to example 46 from 2-(3-ethylmercapto-propoxy)-4-methoxy-thio-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 187 to 189°C.

Example 54

2-(2,3,4-Trimethoxy-phenyl)-1H-imidazo/4,5-b/-pyridine-hydrochloride

Prepared analogous to example 28 from 2,3,4-trimethoxy-thio-benzoic acid-morpholide-methoiodide (m.p.: 147 to 150°C) and 2,3-diamino-pyridine.

M.p.: 231 to 233°C (decomp.).

Example 55

2-(2-Methoxy-3,4-methylenedioxy-phenyl)-1H-imidazo/4,5-b/pyridine-hydrochloride

Prepared analogous to example 28 from 2-methoxy-3,4-methylenedioxy-thio-benzoic acid-morpholide-methoiodide (m.p.: 109 to 111°C) and 2,3-diaminopyridine.

M.p.: 266 to 268°C.

Example 56

2-(2,4-Dimethoxy-3-hydroxy-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2,4-dimethoxy-3-hydroxy-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 115 to 118°C.

Example 57

2-(2-Methoxy-4-chloro-phenyl)-1H-imidazo[4,5-b]pyridine-hydro-chloride

Prepared analogous to example 28 from 2-methoxy-4-chloro-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 302 to 305°C.

Example 58

2-(2-Methoxy-4-methyl-phenyl)-1H-imidazo[4,5-b]pyridine-hydro-chloride

Prepared analogous to example 28 from 2-methoxy-4-methyl-thio-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 256°C (decomp.).

Example 59

2-(2-Ethoxy-4-methyl-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2-ethoxy-4-methyl-thio-benzoic

acid-morpholide-methoiddide (m.p.: 142 to 144°C) and 2,3-diamino-pyridine.

M.p.: 224 to 225°C (decomp.).

Example 60

2-(2-Methoxy-4-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 18b) from 2-methoxy-4-methylmercapto-benzoic acid-morpholide (m.p.: 124 to 129°C) and 2,3-diamino-pyridine.

M.p.: 232 to 234°C.

Example 61

2-(2-Methoxy-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 18b) from 2-methoxy-5-methylmercapto-benzoic acid-morpholide (m.p.: 106 to 108°C) and 2,3-diamino-pyridine.

M.p.: 247 to 248°C.

Example 62

2-(2-Methoxy-4-ethylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 25 from 2-methoxy-4-ethylmercapro-benzoic acid-morpholide and 2,3-diaminopyridine.

M.p.: 215 to 217°C.

Example 63

2-(2-Methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2-methylmercapto-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 185 to 187°C.

Example 64

2-(2,4-Bismethylmercapto-phenyl-1H imidazo[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2,4-bismethylmercapto-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 249 to 250°C.

Example 65

2-[2-(2-Methylmercapto-ethoxy)-4-methylmercapto-phenyl]-1H-imidazo-[4,5-b]pyridine-hydrochloride

Prepared analogous to example 28 from 2-(2-methylmercapto-ethoxy)-4-methylmercapto-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 180 to 182°C.

Example 66

2-[2-(2-Diethylamino-ethoxy)-4-methyl-phenyl]-1H-imidazo[4,5-b]-pyridine-hydrochloride

Prepared analogous to example 28 from 2-(2-diethylamino-ethoxy)-4-methyl-thio-benzoic acid-morpholide-methoiodide-hydrochloride and 2,3-diaminopyridine.

M.p.: 221 to 223°C.

Example 67

2-(2-Allyloxy-4-methoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

16.5 g of 2-allyloxy-4-methoxy-benzoyl morpholide and 7.1 g of 2,3-diaminopyridine were powdered and intimately mixed and 30 ml of phosphorus oxychloride were added dropwise whilst stirring. Subsequently, the reaction mixture was refluxed for 3 hours, the excess of phosphorus oxychloride was removed and the residue was decomposed with ice-water. The solution, which had been made alkaline with ammonia, was extracted with chloroform. The organic solution was extracted with 2N hydrochloric acid and the aqueous phase was made alkaline with ammonia and extracted with chloroform. The chloroform solution

was dried, treated with charcoal/tonsil, filtered and evaporated. The residue was dissolved in acetone and the light yellow colored hydrochloride was precipitated with ethereal hydrochloric acid.

M.p.: 189 to 191°C.

Example 68

2-(2,4,5-Trimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

a) 2-(2,4,5-Trimethoxy-phenyl)-1,3-dithiolanium-iodine

50 g of 1.2,4-trimethoxybenzene and 150 g of 2-methylmercapto-1,3-dithiolanium-methyl sulfate were stirred in 600 ml of glacial acetic acid for 4 hours at 70°C bath temperature. Subsequently, the solvent was removed, the residue was dissolved in a mixture of chloroform and water and an excess of potassium iodide solution was added to the aqueous layer, whereby the product precipitated as orange-colored crystals.

b) 2-(2,4,5-Trimethoxy-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

3.8 g of 2-(2,4,5-trimethoxy-phenyl)-1,3-dithiolanium -iodide and 2.2 g of 2,3-diaminopyridine were heated for

10 minutes in 40 ml of glycol at 200°C. After cooling the mixture was extracted with ether and then with chloroform. The chloroform layer was extracted with 2N hydrochloric acid and the precipitated yellow hydrochloride was suction filtered and recrystallised from glycol.

M.p.: 278 to 280°C

Example 69

2-(2,4,6-Trimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

a) 2-(2,4,6-Trimethoxy-phenyl)-1,3-dithiolanium-iodide

33.6g of phloroglucinol-trimethyl ether and 105 g of 2-methylmercapto-1,3-dithiolanium-methyl sulfate were held at 75°C for 6 hours in 200 ml of glacial acetic acid and the crystals which precipitated after standing overnight were suction filtered, dissolved in water and the iodide thereof was precipitated with potassium iodide solution.

M.p.: 153 to 154°C.

b) 2-(2,4,6-Trimethoxy-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

4 g of 2-(2,4,6-trimethoxy-phenyl)-1,3-dithiolanium-iodide, 2.2 g of 2,3-diaminopyridine and 5 g of lead acetate were heated for 10 minutes in 75 ml of glycol. Subsequently the precipitated lead salt was filtered off, the filtrate was diluted with water and the precipitated product was suction filtered. After dissolving in methanolic hydrochloric acid, the product was purified by passage through a silica gel column (eluent: chloroform: methanol = 9:1)

M.p.: 241 to 244°C (from ethanol)

Example 70

2-(2,4-Dihydroxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 69 from 3-hydroxy-4-[1',3'-dithiacyclopentylidene-(2')]-cyclohexadiene-(2,5)-one-(1) and 2,3-diaminopyridine.

M.p.: 298 to 301°C.

A

Example 71

2-(4-Dimethylamino-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 69 from 2(4-dimethylamino-phenyl)-1,3-dithiolanium-iodide and 2,3-diamino-pyridine in n-propanol.

M.p.: 337 to 339°C.

Example 72

2-(2-Methoxy-4-dimethylamino-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

a) 2-(2-Methoxy-4-dimethylamino-phenyl)-1,3-dithiolanium-iodide

22.6 g of 3-dimethylamino-anisole, 43.2 g of 2-methylmercapto-1,3-dithiolanium-methyl sulfate, 150 ml of glacial acetic acid and 22.5 ml of pyridine were refluxed for ½ hour. After cooling, the mixture was poured into an aqueous potassium iodide solution, the precipitated product was suction filtered and dried.

M.p.: 189 to 195°C (from dimethylformamide)

b) 2-(2-Methoxy-4-dimethylamino-phenyl)-1H-imidazo [4,5-b]pyridine hydrochloride

Prepared analogously to Example 42 from 2-(2-methoxy-4-dimethylamino-phenyl)-1,3-dithiolanium-iodide and 2,3-diaminopyridine.

M.p.: 258 to 260°C (from methanol)

Example 73

2-(2-Methylsulfinyl-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

1.35 g of 2-(2-methylmercapto-phenyl)-1H-imidazo [4,5-b]pyridine were dissolved in 20 ml of glacial acetic acid and 0.64 g of 30% hydrogen peroxide dissolved in 5 ml of glacial acetic acid were added dropwise. After standing overnight, the mixture was diluted with water, neutralized with sodium bicarbonate and the precipitated product was suction filtered and dried. By addition of ethereal hydrochloric acid to a methanolic solution of the product the colorless hydrochloride was obtained.

M.p.: 205 to 210°C.

A1

Example 74

2-(2-Methylsulfonyl-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

450 mg of 2-(2-methylmercapto-phenyl)-1H-imidazo [4,5-b]pyridine hydrochloride and 370 mg of 30% hydrogen peroxide were heated for 3 hours at 70°C in 20 ml of glacial acetic acid. After evaporation and trituration with petroleum ether, the desired product crystallized. M.p.: 259 to 262°C (from isopropanol)

Example 75

2-[2-(2-Methylsulfinyl-ethoxy)-phenyl]-1H-imidazo[4,5-b] pyridine hydrochloride

a) 2-[2-(2-Methylmercapto-ethoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

Prepared analogous to example 28 from 2-(2-methylmercapto-ethoxy)-thio-benzoic acid-morpholide-methoiodide and 2,3-diaminopyridine.

M.p.: 138 to 140°C.

b) 2-[2-(2-Methylsulfinyl-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine-hydrochloride

4,3 g of 2-[2-(2-methylmercapto-ethoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine-hydrochloride and 1,5 g of 30 % hydrogen peroxide were stirred for 2 hours at room temperature in 100 ml of glacial acetic acid. After standing over night, the mixture was diluted with water, neutralised with bicarbonate and extracted with chloroform. The chloroform layer was evaporated, the residue was taken up in acetone and the hydrochloride was precipitated with methanolic hydrochloric acid.

M.p.: 163 to 165°C.

Example 76

2-[2-(2-Methylsulfinyl-ethoxy)-4-methoxy-phenyl]-1H-imidazo-[4,5-b]pyridine-hydrochloride

Prepared analogous to example 75b from 2-[2-(2-methylmercapto-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]pyridine-hydrochloride.

M.p.: 231 to 232°C.

Example 77

2-[2-(2-Ethylsulfinyl-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]-pyridine

Prepared analogous to example 75b from 2-[2-(2-ethylmercapto-ethoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b]pyridine-hydrochloride.

M.p.: 188 to 189°C.

Example 78

2-[2-(3-Methylsulfinyl-propoxy)-4-methoxy-phenyl]-1H-imidazo-[4,5-b]pyridine

Prepared analogously to Example 75b from 2-[2-[2-(3-methylmercapto-propoxy)-4-methoxy-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

M.p.: 132 to 133°C

Example 79

2-[2-(3-Ethylsulfinyl-propoxy)-4-methoxy-phenyl]-1H-imidazo [4,5-b]pyridine

Prepared analogously to Example 75b from 2-[2-(3-ethylmercapto-propoxy)-4-methoxy-phenyl]-1H-imidazo[4,5-b] pyridine hydrochloride.

M.p.: 126 to 127°C.

(A)

Example 80

2-(2-Methoxy-4-methylsulfinyl-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

6.6 g of 2-(2-methoxy-4-methylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine were dissolved in 100 ml of chloroform and a solution of 2.96 g of 3-chloro-perbenzoic acid in 600 ml of chloroform was dropped in at -15 to -20°C during 5 hours. Subsequently, the mixture was extracted with a dilute sodium carbonate solution and the chloroform layer was dried and evaporated. The residue was purified over a silica gel column (eluent: chloroform/methanol = 9:1). By addition of ethereal hydrochloric acid to a methanolic solution of the base the yellow hydrochloride was obtained.

M.p.: 154 to 155°C.

Example 81

2-(2-Methoxy-4-methylsulfonyl-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

Prepared analogously to Example 74 from 2-(2-methoxy-4-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride.

M.p.: 240 to 242°C.

Example 82

2-(2-Methoxy-4-ethylsulfinyl-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride

Prepared analogously to Example 80 from 2-(2-methoxy-4-ethylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine

M.p.: 121 to 123°C

Example 83

2-[2-(2-Methylsulfinyl-ethoxy)-4-methylmercapto-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 80 from 2-[2-methylmercapto-ethoxy)-4-methylmercapto-phenyl]-1H-imidazo [4,5-b]pyridine and an equimolar quantity of 3-chloro-perbenzoic acid.

M.p.: 191 to 192°C (from acetone)

Example 84

2-[2-(2-Methylsulfinyl-ethoxy)-4-methylsulfinyl-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 80 from 2-[2-(2-methylsulfinyl-ethoxy)-4-methylmercapto-phenyl]-1H-imidazo [4,5-b]pyridine and an equimolar quantity of 3-chloro-perbenzoic acid.

M.p.: 190 to 191°C.

Example 85

2-[2-(2-Methylsulfinyl-ethoxy)-4-methyl-phenyl]-1H-imidazo [4,5-b] pyridine hydrochloride

Prepared analogously to Example 75b from 2-[2-(2-methylmercapto-ethoxy)-4-methyl-phenyl]-1H-imidazo[4,5-b] pyridine hydrochloride.

M.p.: 191 to 192°C (from acetone/ether).

Example 86

2-[2-(2-Methylsulfinyl-ethoxy)-4-chlorophenyl]-1H-imidazo [4,5-b] pyridine hydrochloride

Prepared analogously to Example 75b from 2-[2-(2-methymercapto-ethoxy)-4-chloro-phenyl]-1H-imidazo[4,5-b] pyridine hydrochloride.

M.p.: 221 to 222°C (from acetone/ether).

Example 87

2-[2-Methoxy-4-(2-methylsulfinyl-ethoxy)-phenyl]-1H-imidazo [4,5-b]pyridine

Prepared analogously to Example 75 b from 2-[2-methoxy-4-(2-methylmercapto-ethoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride.

M.p.: 204 to 205°C.

Example 88

2-[2-Methoxy-4-(2-ethylsulfinyl-ethoxy)-phenyl]-1H-imidazo [4,5-b] pyridine

Prepared analogously to Example 75b from 2-[2-methoxy-4-(2-ethyl-mercapto-ethoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride.

M.p.: 217 to 219°C

Example 89

2-[2-Methoxy-4-(3-methylsulfinyl-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 75b from 2-[2-methoxy-4-(3-methylmercapto-propoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride.

M.p.: 179 to 180°C.

Example 90

2-[2-Methoxy-4-(3-ethylsulfinyl-propoxy)-phenyl]-1H-imidazo [4,5-b] pyridine hydrochloride

Prepared analogously to Example 75b from 2-[2-methoxy-4-(3-ethylmercapto-propoxy)-phenyl]-1H-imidazo [4,5-b]pyridine hydrochloride

M.p.: 167 to 168°C.

[A]

Example 91

2-(2-Methoxy-5-methylsulfinyl-phenyl)-1H-imidazo[4,5-b] pyridine

Prepared analogously to Example 80 from 2-(2-methoxy-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride.

M.p.: 211 to 212°C.

Example 92

2-(2-Methoxy-5-methylsulfonyl-phenyl)-1H-imidazo[4,5-b] pyridine

Prepared analogously to Example 74 from 2-(2-methoxy-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

M.p.: 240 to 241°C.

Example 93

2-(2,4-Dimethoxy-phenyl-1H-imidazo[4,5-b]pyridine-oxide-(4)

1 g of 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b] pyridine and 1.35 g of 3-chloroperbenzoic acid were stirred for 15 hours at 60°C in 15 ml of glacial acetic acid. Subsequently, the mixture was recrystallized from

2N acetic acid by addition of charcoal. The further purification was effected by boiling with acetone.

M.p.: 266 to 267°C.

Example 94

2-(2,4-Dimethoxy-phenyl)-3-methyl-3H-imidazo[4,5-b] pyridine hydrochloride

3.6 g of methyl iodide were added dropwise to a solution of 3.5 g of 2-(2,4-dimethoxy-phenyl)-1H-imidazo [4,5-b]pyridine hydrochloride and 27 g of potassium tert.-butoxide in 40 ml of dimethylformamide. The mixture was stirred for 2 hours at room temperature and then evaporated. The residue was dissolved in chloroform/water, the organic layer was separated, dried and evaporated. The product was purified by column chromatography and subsequently precipitated from the solution in acetone with ethereal hydrochloric acid.

M.p.: 196 to 197°C.

Example 95

2-(2-Hydroxy-phenyl)-3-methyl-3H-imidazo [4,5-b]pyridine hydrochloride

Prepared analogously to Example 94 from 2-(2-hydroxy-phenyl)-1H-imidazo[4,5-b]pyridine and methyl iodide.

M.p.: 215 to 216°C.

Example 96

2-(2-Hydroxy-4-methoxy-phenyl)-3-(3-hydroxypropyl)-3H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 94 from 2-(2-hydroxy-4-methoxy-phenyl)-1H-imidazo[4,5-b]pyridine and 3-bromo-propanol.

M.p.: 154 to 155°C.

Example 97

2-(2,4-Dimethoxy-phenyl)-3-benzyl-3H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 94 from 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine and benzyl bromide.

M.p.: 148 to 150°C.

Example 98

2-(2-Dimethoxy-phenyl)-3-(2-diethylaminoethyl)-3H-imidazo-[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 94 from 2-(2-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine and 2-diethylamino-ethyl chloride at 80°C.

M.p.: 185°C.

Example 99

2-(2,4-Dimethoxy-phenyl)-3-(3-dimethylaminopropyl)-3H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 94 from 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine and 3-dimethylaminopropyl bromide at 70°C.

M.p.: 190 to 192°C (decomp.).

Example 100

2-(2-Methoxy-4-benzyloxy-phenyl)-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 10 from 2-methoxy-4-benzyloxy-benzoyl morpholide and 2,3-diamino-pyridine.

M.p. of the hydrochloride: 218 to 219°C (decomp.).

Example 101

2-(2,4-Dimethoxy-phenyl)-3-butyl-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 10 from 2,4-dimethoxy-benzoyl morpholide and 3-amino-2-butylamino-pyridine.

M.p. of the hydrochloride: 218 to 219°C.

A

Example 102

2-(2-Methoxy-4-hydroxy-phenyl)-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 10 from 2-methoxy-4-hydroxy-benzoyl morpholide and 2,3-diamino-pyridine.

M.p. of the hydrochloride: 230 to 231°C.

Example 103

2-(2-Ethoxy-4-ethylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 10 from 2-ethoxy-4-ethylmercapto-benzoyl morpholide and 2,3-diamino-pyridine.

M.p. of the hydrochloride: 198 to 199°C (decomp.).

Example 104

2[4-Methoxy-2-(3-(4-methyl-1-piperazinyl)-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 21 from 2-[4-methoxy-2-(3-chloro-propoxy)-phenyl]-1H-imidazo[4,5-b] pyridine and 1-methylpiperazine.

M.p. of the trihydrochloride: 248°C (decomp.)

Example 105

2-[4-Methoxy-2-(2-thiomorpholine-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 21 from 2-[4-methoxy-2-(2-chloro-ethoxy)-phenyl]-1H-imidazo[4,5-b]-

-pyridine and thiomorpholine.

M.p.: 158 to 160°C.

Example 106

2-(2-Fluoro-4-methoxy-phenyl)-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 1 from 2-fluoro-4-methoxy-benzoic acid and 2,3-diamino-pyridine.

M.p. of the hydrochloride: 237 to 238°C (decomp.).

Example 107

2-(4-Fluoro-2-methoxy-phenyl)-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 1 from 4-fluoro-2-methoxy-benzoic acid and 2,3-diamino-pyridine.

M.p. of the hydrochloride: 235 to 236°C (decomp.)

Example 108

2-(2-Hydroxy-4-methoxy-phenyl)-3-phenyl-3H-imidazo-[4,5-b]pyridine

4.9 g of 2-hydroxy-4-methoxy-benzanilide and 2.6 g of 2-chloro-3-amino-pyridine were refluxed for 1½ hours in 50 ml of phosphorus oxychloride. After distilling

off the excess of phosphorus oxychloride the residue was boiled for 45 minutes with 2N hydrochloric acid, neutralized with ammonia and the precipitated product was recrystallized from isopropanol.

M.p.: 201°C.

Example 109

2-(2-Hydroxy-4-methoxy-phenyl)-3-(2-methoxy-phenyl)-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 108 from N-(2-methoxy-phenyl)-2-hydroxy-4-methoxy-benzamide and 2-chloro-3-amino-pyridine.

M.p.: 197°C.

Example 110

2-(2-Hydroxy-4-methoxy-phenyl)-3-(4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 108 from N-(4-methoxy-phenyl)-2-hydroxy-4-methoxy-benzamide and 2-chloro-3-amino-pyridine.

M.p.: 175°C.

Example 111

2-(2-Hydroxy-4-methoxy-phenyl)-3-(2-phenylethyl)-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 108 from

N-(2-phenylethyl)-2-hydroxy-4-methoxy-benzamide and 2-chloro-3-amino-pyridine.

M.p.: 155°C.

Example 112

2-(2,4-Dimethoxy-phenyl)-3-phenyl-3H-imidazo[4,5-b]pyridine

Prepared from N-phenyl-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine by heating for 5 minutes with sodium hydride in dimethylformamide at 120°C.

M.p.: 138°C (from cyclohexane/isopropanol = 9/1).

Example 113

2-(2,4-Dimethoxy-phenyl)-3-(2-methoxy-phenyl)-3H-imidazo-[4,5-b]pyridine

Prepared analogously to Example 112 from N-(2-methoxy-phenyl)-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine.

M.p.: 156°C.

C

Example 114

2-(2,4-Dimethoxy-phenyl)-3-(4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 112 from N-(4-methoxy-phenyl)-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine.

M.p.: 163°C.

Example 115

2-(2,4-Dimethoxy-phenyl)-3-(3,4-dimethoxy-phenyl)-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 112 from N-(3,4-dimethoxy-phenyl)-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine.

M.p.: 190°C.

Example 116

2-(3,4-Dimethoxy-phenyl)-3-(4-methoxy-phenyl)-3H-imidazo-[4,5-b]pyridine

Prepared from N-(4-methoxy-phenyl)-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine analogously to Example 112 or by boiling in chlorobenzene.

M.p.: 181°C.

Example 117

2-(2,4-Dimethoxy-phenyl)-3-(3-morpholino-1-propyl)-3H-imidazo[4,5-b]pyridine

A

Prepared analogously to Example 112 from

N-(3-morpholino-1-propyl)-N'-(2-chloro-3-pyridyl)-2,4-dimethoxy-benzamidine.

M.p.: 207°C.

Example 48

2-(2,6-Dimethoxyphenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

9.1 g of 2,6-dimethoxy-benzoic acid and 5.5 g of 2,3-diaminopyridine were refluxed for 3 hours in 100 ml of phosphorus oxychloride. Subsequently the excess of phosphorus oxychloride was distilled off and the residue was carefully decomposed with ice-water. The obtained solution was filtered, neutralized with potassium carbonate and made alkaline with concentrated ammonia. The suspension which formed was extracted three times with chloroform. The chloroform layer was dried over magnesium sulfate, filtered and the solvent was removed. The remaining residue was dissolved in 50 ml of methanolic hydrochloric acid, subsequently 100 ml of isopropanol were added and the product was kept in the deep freezer overnight. The precipitate was suction filtered and washed with ether.

M.p.: 250 to 254°C.

A

Example 119

2-(2-Propoxy-4-methyl-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 118 from 2-propoxy-4-methyl-benzoyl morpholide.

M.p.: 221 to 223°C. (decomp.).

Example 120

2-(2-Butoxy-4-methyl-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 118 from 2-butoxy-4-methyl-benzoyl morpholide.

M.p.: 212 to 213°C (decomp.).

Example 121

2-(4-Methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example 118 from 4-methyl-mercaptobenzoic acid.

M.p.: 230 to 232°C.

Example 122

2-[2-(2-Methylmercapto-ethoxy)-5-methylmercapto-phenyl]-1H-imidazo[4,5-b]pyridine hydrochloride

50 g of S-methyl-[2-(2-methylmercapto-ethoxy)-5-methylmercapto]-thiobenzoyl morpholide iodide (obtained by reaction of [2-(2-methylmercapto-ethoxy)-5-methylmercapto]-

-thiobenzoyl morpholide with methyl iodide in methanol) and 15 g of 2,3-diaminopyridine were heated for 3 hours at 130°C in 150 ml of glycol. After cooling, the mixture was diluted with water and 30 ml of concentrated ammonia were added. Subsequently, the mixture was extracted with chloroform, the organic layer was washed with water and 2N hydrochloric acid was added. The precipitate was suction filtered and recrystallised from methanol.

M.p.: 190 to 191°C.

C

Example 123

2-(2-Methoxy-4-propylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine hydrochloride

Prepared analogously to Example 118 from 2-methoxy-4-propylmercapto-benzoyl morpholide.

M.p.: 203 to 204°C (decomp.).

Example 124

2-(2-Ethoxy-4-propylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine hydrochloride

Prepared analogously to Example 118 from 2-ethoxy-4-propylmercapto-benzoyl morpholide.

M.p.: 182 to 183°C.

[A]

Example 125

2-(2-Methoxy-4-butylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine hydrochloride

Prepared analogously to Example 116 from 2-methoxy-4-butylmercapto-benzoyl morpholide.

M.p.: 203 to 204°C.

Example 126

2-(2-Ethoxy-4-butylmercapto-phenyl)-H-imidazo[4,5-b]-pyridine hydrochloride

Prepared analogously to Example 116 from 2-ethoxy-4-butylmercaptobenzoyl morpholide.

M.p.: 207 to 208°C.

Example 127

2-(4-Methylsulfinyl-phenyl)-1H-imidazo[4,5-b]pyridine

5.9 g of 2-(4-methylmercapto-phenyl)-1H-imidazo-[4,5-b]pyridine hydrochloride were dissolved in 100 ml of glacial acetic acid and 2.4 g of 30% hydrogen peroxide were added at 10°C. Subsequently the mixture was stirred for 3 hours, and then left to stand overnight in the refrigerator and for 10 hours at laboratory temperature. The mixture was made alkaline with ammonia and was extracted several times with chloroform. The starting material was separated by column chromatography. The residue was suspended in acetone and the crystals

which formed were suction filtered.

M.p.: 240 to 242°C.

Example 128

2-(2-Ethoxy-5-methylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 127 from 2-(2-ethoxy-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine.

M.p.: 197 to 198°C.

Example 129

2-[2-(2-Methylsulfinyl-ethoxy)-5-methylmercapto-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example 127 from 2-[2-(2-methylmercapto-ethoxy)-5-methylmercapto-phenyl]-1H-imidazo[4,5-b]pyridine hydrochloride.

M.p.: 189 to 190°C.

Example 130

2-(2-Ethoxy-4-ethylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 127 from 2-(2-ethoxy-4-ethylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride.

M.p.: 166 to 167°C.

[A]

Example 131

2-(2-Methoxy-4-propylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 127 from 2-(2-methoxy-4-propylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine hydrochloride.

M.p.: 182 to 183°C.

Example 132

2-(2-Ethoxy-4-propylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 127 from 2-(2-ethoxy-4-propylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride.

M.p.: 182 to 183°C (decomp.).

Example 133

2-(2-Ethoxy-4-butylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 127 from 2-(2-ethoxy-4-butylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride.

M.p.: 185 to 186°C.

Example 134

2-(4-Methylsulfonyl-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

6.95 g of 2-(4-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride were dissolved in 100 ml of glacial acetic acid, 8.5 g of 30% hydrogen peroxide were added and the mixture was left standing for 4 days at room temperature. After purification by passage through a silica gel column, the residue was dissolved in acetone and the hydrochloride was precipitated with methanolic hydrochloric acid.

M.p.: 286°C.

Example 135

2-(2-Ethoxy-4-ethylsulfonyl-phenyl)-1H-imidazo[4,5-b]-pyridine

400 mg of 2-(2-ethoxy-4-ethylmercapto-phenyl)-1H-imidazo[4,5-b] pyridine hydrochloride were dissolved in 30 ml of glacial acetic acid together with 0.5 ml of 30% hydrogen peroxide. The mixture was allowed to stand overnight and was then heated for 1 hour at 90°C. After cooling, the mixture was diluted with water, neutralized with bicarbonate, extracted with chloroform and the organic layer was evaporated after drying. The residue was purified by column chromatography.

M.p.: 207 to 208°C (from acetone).

[A]

C

Example ~~136~~ 136

2-(2-Methoxy-4-propylsulfonyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example ~~137~~ 135 from 2-(2-methoxy-4-propylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine.

M.p.: 219 to 220°C.

Example ~~138~~ 137

2-(2-Ethoxy-4-butylsulfonyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example ~~139~~ 135 from 2-(2-ethoxy-4-butylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine.

M.p.: 156 to 157°C.

Example ~~140~~ 138

2-[2-Methoxy-4-(2-dimethylamino-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

a) 2-[2-Methoxy-4-(2-chloroethoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine hydrochloride

14 g of 2-methoxy-4-(2-hydroxyethoxy)-benzoyl morpholide were refluxed for 1½ hours with 7.1 g of 2,3-diaminopyridine in 100 ml of phosphorus oxychloride. Subsequently the mixture was decomposed with ice-water. The gradually crystallizing precipitate was suction

A

filtered and washed with acetone.

M.p.: 266 to 268°C (decomp.).

b) 2 g of 2-[2-methoxy-4-(2-chloroethoxy)-phenyl]-1H-imidazo[4,5-b] pyridine hydrochloride were heated in a closed vessel for 12 hours at 120°C with 5 g of dimethylamine in 100 ml of ethanol. After evaporation, the residue was purified by column chromatography. The hydrochloride was precipitated from acetone with methanolic hydrochloric acid and subsequently recrystallized from methanol.

M.p.: > 250°C.

Example 139

2-[2-Methoxy-4-(3-dimethylamino-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 140 from 2-[2-methoxy-4-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine hydrichloride.

M.p.: 238 to 242°C.

Example 140

2-[2-Methoxy-4-(3-diethylamino-propoxy)-phenyl]-1H-imidazo[4,5-b] pyridine dihydrochloride

Prepared analogously to Example 138 from 2-[2-methoxy-4-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine hydrochloride.

M.p.: 222 to 224°C.

Example 141

2-[2-Methoxy-4-(3-piperidino-propoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 139 from 2-[2-methoxy-4-(3-chloropropoxy)-phenyl]-1H-imidazo-[4,5-b]pyridine hydrochloride.

M.p.: 225 to 226°C (decomp.).

Example 142

2-[2-Methoxy-4-(3-(4-phenyl-piperazin-1-yl)-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 139 from 2-[2-methoxy-4-(3-chloro-propoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine hydrochloride.

M.p.: 197 to 200°C.

Example 143

2-[2-Methoxy-4-(3-(4-(2-methoxyphenyl)-piperzin-1-yl)-propoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine trihydrochloride hydrate

A1

Prepared analogously to Example 139 from 2-[2-methoxy-4-(3-chloro-propoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine hydrochloride.

M.p.: Sintering from 180°C.

Example 144

2-(2-Methoxy-4-morpholino-phenyl)-1H-imidazo[4,5-b]-pyridine hydrochloride

a) 2-(2-Methoxy-4-morpholino-phenyl)-1,3-dithiolanium-iodide

10.5 g of 3-morpholino-anisole and 15.7 g of 2-methylmercapto-1,3-diethiolanium-methyl sulfate were boiled in a mixture of 60 ml of glacial acetic acid and 8.3 ml of pyridine for 1 hour. After cooling, the mixture was poured into a saturated potassium iodide solution. The red precipitate was suction filtered and washed with water. The product was used without further purification.

b) 22 g of 2-(2-methoxy-4-morpholino-phenyl)-1,3-dithiolanium iodide, 10.9 g of 2,3-diaminopyridine and 60 ml of glycol were heated for 2 hours at 130°C. After cooling, water was added and the mixture was extracted with chloroform. After evaporation, the residue was purified by column chromatrography and the hydrochloride was precipitated from acetone with ether/hydrochloride acid.

M.p.: 207 to 209°C (decomp.).

C

Example ~~142~~ 145

2-[2-Methoxy-4-(4-methyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b] pyridine dihydrochloride

Prepared analogously to Example ~~142~~ 144 from 3-(4-methyl-piperazin-1-yl)-anisole.

M.p.: 279 to 282°C.

Example ~~143~~ 146

2-[2-Methoxy-4-(4-ethyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example ~~143~~ 144 from 3-(4-ethyl-piperazin-1-yl)-anisole.

M.p.: 218 to 222°C.

A

C

Example ~~150~~ 147

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2-[2-Methoxy-4-(4-propyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example ~~147~~ 144 from 3-(4-propyl-piperazin-1-yl)-anisole.

M.p.: 256 to 258°C.

Example ~~151~~ 148

2-[2-Ethoxy-4-(4-methyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example ~~147~~ 144 from 3-(4-methyl-piperazin-1-yl)-1-ethoxybenzene.

M.p.: 269 to 271°C.

Example ~~152~~ 149

2-[2-Ethoxy-4-(4-ethyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]-pyridine dihydrochloride

Prepared analogously to Example ~~147~~ 144 from 3-(4-ethyl-piperazin-1-yl)-1-ethoxybenzene.

M.p.: 257 to 259°C.

Example ~~153~~ 150

2-[2-Methoxy-4-(4-phenyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example ~~147~~ 144 from 3-(4-phenyl-piperazin-1-yl)-anisole.

M.p.: 217 to 219°C.

[A]

C

Example 151

2-[4-Methoxy-2-(2-morpholino-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared from 6.3 g of 2-[4-methoxy-2-(2-chloro-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine by refluxing for 3 hours in 60 ml of morpholine, distilling off the excess of morpholine in vacuo and recrystallizing the residue from isopropanol.

M.p.: 188 to 190°C.

Example 152

2-[4-Methoxy-2-(3-(4-phenyl-piperazin-1-yl)-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

10 g of 2-[4-methoxy -2-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]pyridine, 10.2 g of 1-phenyl-piperazine and 5 g of potassium carbonate were refluxed for 8 hours in 100 ml of ethanol. After distilling off the ethanol in vacuo, the mixture was recrystallized from ethanol/water 3:1.

M.p.: 162 to 163°C.

Example 153

2-[4-Methoxy-2-(3-(2-phenyl-ethylamino)-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared by heating 1.77 g of 2-[4-methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]pyridine in 10 ml of 2-phenyl-ethylamine for 1½ hours at 180°C. The free base was converted into the dihydrochloride with methanolic hydrochloric acid. Recrystallization from isopropanol.

M.p.: 238°C.

Example ~~151~~ 159

2-[4-methoxy-2-(3-(N-methyl-N-2-phenylethyl-amino)-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared from 3.2 g of 2-[4-methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]pyridine and 2.7 g of N-methyl-2-phenyl-ethylamine by heating for 6 hours in ethanol at 120°C in a closed vessel. The dihydrochloride was precipitated with ethereal hydrochloric acid from an ethyl acetate solution of the base, purified by column chromatography and recrystallized from isopropanol.

M.p.: 212 to 215°C.

Example ~~152~~ 165

2-[4-Methoxy-2-(3-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)-amino)-propoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine dihydrochloride

Prepared from 5.0 g of 2-[4-methoxy-2-(3-chloro-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine and 8.5 g of N-[2-(3,4-dimethoxy-phenyl)-ethyl]-methylamine by refluxing for 12 hours in ethylene glycol monomethyl ether. Precipitation of the dihydrochloride from ethyl acetate with ethereal hydrochloric acid.

M.p.: 169°C.

C

Example ~~149~~ 152

2-[4-Methoxy-2-(3-thiomorpholino-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared analogously to Example ~~150~~ 153 from 2-[4-methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine and thiomorpholine by heating for 30 hours. Purification was by precipitation of the maleate from ethyl acetate solution. The free base was obtained from the maleate with 2N ammonia.

M.p.: 111°C.

Example ~~151~~ 154

2-[4-Methoxy-2-(2-(4-methyl-piperazin-1-yl)-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine

Prepared from 3.0 g of 2-[4-methoxy-2-(2-chloro-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine and 2.0 g of N-methylpiperazine by refluxing for 40 hours in

[A]

ethanol. After purification by column chromatography over silica gel, the product was recrystallized from water.

M.p.: 136 to 137°C.

C

Example ~~161~~ 157

2-[4-Methoxy-2-(3-(4-(2-phenylethyl)-piperazin-1-yl)-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine trihydrochloride

Prepared analogously to Example ~~159~~ 154 from 2-[4-methoxy-2-(3-chloro-propoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine and 1-(2-phenyl-ethyl)-piperazine.

M.p.: 236 to 238°C.

Example ~~162~~ 159

2-[4-Methoxy-2-(3-methylamino-propoxy)-phenyl]-1H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example ~~157~~ 154 from 2-[4-methoxy-2-(3-chloropropoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine and methylamine.

M.p.: 215°C.

Example ~~163~~ 160

2-[4-Methoxy-2-(2-dimethylamino-ethoxy)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

A

C

Prepared analogously to Example ~~159~~ 154 from 2-[4-methoxy-2-(2-chloro-ethoxy)-phenyl]-1H-imidazo[4,5-b]-pyridine and dimethylamine.

M.p.: 240 to 242°C.

Example ~~162~~ 161

2-(2-Methylamino-phenyl)-1H-imidazo[4,5-b]pyridine

1.77 g of N-methyl-isatinoyl anhydride and 1.09 g of 2,3-diaminopyridine were melted and heated for 10 minutes at 180°C. Recrystallization from ethyl acetate.

M.p.: 262 to 263°C.

Example ~~165~~ 163

2-(2,4-Dimethoxy-phenyl)-3-(2-phenyl-ethyl)-3H-imidazo-[4,5-b]pyridine

0.17 g of 2-(2-hydroxy-4-methoxy-phenyl)-3-(2-phenyl-ethyl)-3H-imidazo[4,5-b]pyridine were dissolved in 7 ml of dimethylformamide. The mixture was stirred for 5 minutes with 0.02 g of sodium hydride (80% suspension in oil) and reacted with 0.07 g of methyl iodide under ice-cooling. After 4 hours, water was added to the reaction mixture. The precipitated product was dissolved in ethyl acetate, and the organic layer was washed with 2N sodium hydroxide solution and water

A

and evaporated.

Recrystallization from ethanol/water.

M.p.: 157°C.

Example ~~162~~ 163

2-(2,4-Dimethoxy-phenyl)-3-[2-(3,4-dimethoxy-phenyl)-ethyl]-3H-imidazo[4,5-b]pyridine hydrochloride

Prepared analogously to Example ~~120~~ 118 from 3-amino-2-[2-(3,4-dimethoxy-phenyl)-ethylamino]pyridine and 2,4-dimethoxy-benzoic acid. The hydrochloride was precipitated from ether.

M.p.: 195°C.

Example ~~163~~ 164

2-(2-Fluoro-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example ~~120~~ 118 from 2,3-diaminopyridine and 2-fluoro-5-methylmercapto-benzoic acid.

M.p.: 195°C.

Example ~~164~~ 165

2-(2-Fluoro-5-methylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared from 2-(2-fluoro-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine by oxidation with hydrogen

[A]

peroxide in glacial acetic acid at room temperature. The purification was effected by column chromatography on silica gel with chloroform/methanol 19:1 as eluent.

M.p.: 190 to 192°C.

Example ~~169~~ 166

2-(2-Fluoro-5-methylsulfonyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared from 2-(2-fluoro-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine according to Example ~~168~~ 165, but at 40°C.

M.p.: 242°C.

Example ~~170~~ 167

2-(3,4-Dimethoxyphenyl)-3-(3-morpholino-propyl)-3H-imidazo-[4,5-b]pyridine dihydrochloride

a) N-(2-Chloro-3-pyridyl)-N'-(3-morpholinopropyl)-3,4-dimethoxy-benzamidine

4.9 g of N-(3-morpholinopropyl)-3,4-dimethoxy-benzamide and 2.04 g of 2-chloro-3-aminopyridine were refluxed for 2 hours in 85 ml of phosphorus oxychloride. After distilling off the excess of phosphorus oxychloride, the mixture was poured into water. The solution was made alkaline and extracted with ethyl acetate. After

evaporation of the residue, the product remained as viscous oil.

b) 2-(3,4-Dimethoxyphenyl)-3-(3-morpholino-propyl)-3H-imidazo[4,5-b]pyridine dihydrochloride

5.2 g of N-(2-chloro-3-pyridyl)-N'-(3-morpholino-propyl)-3,4-dimethoxy-benzamidine and 1.5 g of sodium hydride (80% suspension in oil) were heated in 100 ml of dimethylformamide for 2 hours at 120°C. The dihydrochloride was precipitated from ether with hydrochloric acid and recrystallized from ethanol/cyclohexane.

M.p.: 180°C.

Example 166

2-(4-Methoxy-phenyl)-3-(3-morpholino-propoxy)-3H-imidazo-[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 167 from N-(2-chloro-3-pyridyl)-N'-(3-morpholino-propyl)-5-methoxy-benzamidine.

M.p.: 218°C.

Example 169

2-(4-Methoxy-phenyl)-3-[3-(4-phenyl-piperazin-1-yl)-propyl]-3H-imidazo[4,5-b]pyridine dihydrochloride hydrate

Prepared analogously to Example 167 from N-(2-chloro-3-pyridyl)-N'-[3-(4-phenyl-piperazin-1-yl)-

A

-propyl]-4-methoxy-benzamidine.

M.p.: 100°C.

Example ~~173~~ 170

2-(4-Methoxy-phenyl)-3(2-morpholino-ethyl)-3H-imidazo-[4,5-b]pyridine hydrochloride

Prepared analogously to Example ~~170~~ 167 from N-(2-chloro-3-pyridyl)-N'-(2-morpholino-ethyl)-4-methoxy-benzamidine.

M.p.: 149°C.

Example ~~174~~ 171

2-(4-Methoxy-phenyl) 3-[3-(4-methyl-piperazin-1-yl)-propyl]-3H-imidazo[4,5-b]pyridine trihydrochloride

Prepared analogously to Example ~~170~~ 167 from N-(2-chloro-3-pyridyl)-N'-[3-(4-methyl-piperazin-1-yl)-propyl]-4-methoxy-benzamidine.

M.p.: 257°C.

Example ~~175~~ 172

2-(4-Methoxy-phenyl)-3-[2-(4-methyl-piperazin-1-yl)-ethyl]-3H-imidazo[4,5-b]pyridine trihydrochloride

Prepared analogously to Example ~~170~~ 167 from N-(2-chloro-3-pyridyl)-N'-[2-(4-methyl-piperazin-1-yl)-ethyl]-4-methoxy-benzamidine.

M.p.: 225°C.

C

A

Example 173

2-(4-Methoxy-phenyl)-3-(3-dimethylamino-propyl)-3H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example 167 from N-(2-chloro-3-pyridyl)-N'-(3-dimethylamino-propyl)-4-methoxy-benzamidine.

M.p.: 229°C.

Example 174

2-(4-Methoxy-phenyl)-3-(3-piperidino-propyl)-3H-imidazo-[4,5-b]-pyridine dihydrochloride

Prepared analogously to Example 167 from N-(2-chloro-3-pyridyl)-N'-(3-piperidino-propyl)-4-methoxy-benzamidine.

M.p.: 196°C.

Example 175

2-(4-Methoxy-phenyl)-3-(4-morpholino-butyl)-3H-imidazo-[4,5-b]pyridine dihydrochloride hydrate

Prepared analogously to Example 167 from N-(2-

chloro-3-pyridyl)-N'-(4-morpholino-butyl)-4-methoxy-benzamidine.

M.p.: 136°C.

Example 176

2-(2-Fluoro-4-methylmercapto-phenyl)-1H-imidazo[4,5-b]-pyridine hydrochloride

Prepared analogously to Example 118 from 2-fluoro-4-methyl-mercapto-benzoic acid and 2,3-diaminopyridine.

M.p.: 257°C.

Example 177

2-(2-Fluoro-4-methylsulfinyl-phenyl)-1H-imidazo[4,5-b]-pyridine

Prepared analogously to Example 165 from 2-(2-

fluoro-4-methyl-mercapto-phenyl)-1H-imidazo[4,5-b]-pyridine. Crystallisation by trituration in petroleum ether.

M.p.: 219°C.

Example 178

2-(4-Methylmercapto-phenyl)-3-(3-morpholino-propyl)-3H-imidazo[4,5-b]pyridine

Prepared analogously to Example 167 from N-(2-chloro-3-pyridyl)-N'-(3-morpholino-propyl)-4-methyl-mercapto-benzamidine. Recrystallized from ether/cyclohexane.

M.p.: 110°C.

Example ~~196~~ 179

2-[2-Propoxy-4-(4-methyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]pyridine dihydrochloride

Prepared analogously to Example ~~147~~ 144 from 3-(4-methyl-piperazin-1-yl)-1-propoxy-benzene.

M.p.: 237 to 238°C.

Example ~~197~~ 180

Tablets containing 100 mg of 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

Composition:

1 tablet contains:

Active ingredient	100.0 mg
lactose	50.0 mg
polyvinyl pyrrolidone	5.0 mg
carboxymethylcellulose	19.0 mg
magnesium stearate	1.0 mg
	175.0 mg
moist screening:	1.5 mm
Drying:	in the circulating air drier at 50°C.
Dry screening:	1 mm

The dry granulate was admixed with the remaining auxiliary products and pressed into tablets.

Weight of tablet:	175 mg
Punch:	8 mm ø

Example ~~106~~ 181

Coated tablets containing 50 mg of 2-(2,4-dimethoxyphenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

1 coated tablet core contains:

Active ingredient	50.0 mg
corn starch, dried	20.0 mg
soluble starch	2.0 mg
carboxymethylcellulose	7.0 mg
magnesium stearate	1.0 mg
	80.0 mg

The active ingredient and corn starch were homogeneously moistened with the aqueous solution of the soluble starch.

Moist screening: 1.0 mm

Dry screening: 1.0 mm

Drying: at 50°C in the circulating air drier

The granulate and the remaining auxiliary products were mixed and pressed to form coated tablet cores.

Weight of core: 80 mg

Punch: 6 mm, arched (5 mm)

The finished cores were covered with a coat consisting essentially of sugar and talcum in conventional manner. The finished coated tablets were polished with

beeswax.

C Weight of the coated tablet: 120 mg

Example 182

Suppositories containing 75 mg of 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

1 suppository contains:

Active ingredient	75.0 mg
B suppository mass (e.g. Witepsol* H 19 and Witepsol* W 45)	1 625.0 mg
	1 700.0 mg

Method of preparation:

The suppository mass was melted. At 38°C the pulverized active ingredient was homogeneously dispersed in the melt. The suppository mass was cooled to 35°C and poured into pre-cooled moulds.

Weight of suppository: 1.7 g

Example ~~184~~ 183

Ampoules containing 50 mg of 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride

1 ampoule contains:

Active ingredient		50.0 mg
sorbitol		250.0 mg
distilled water	ad	5.0 ml

[A]

* Trademark

Method of preparation:

The active ingredient and the sorbitol were dissolved in distilled water. The solution was made up to the given volumn and filtered sterile.

Filling: into ampoules of 5 ml capacity

Sterilisation: 20 minutes at 120°C.

Example 184

Drop solution containing 25 mg of 2-(2,4-dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine hydrochloride per 5 ml

Active ingredient		5.0	g
methyl p-hydroxybenzoate		0.035	g
propyl p-hydroxybenzoate		0.015	g
aniseed oil		0.05	g
menthol		0.06	g
sodium saccharine		1.0	g
glycerine		10.0	g
ethanol		40.0	g
distilled water	ad	100.0	ml

Method of preparation:

The benzoic acid esters were dissolved in ethanol and subsequently the aniseed oil and the menthol were added. Active ingredient, glycerine and sodium

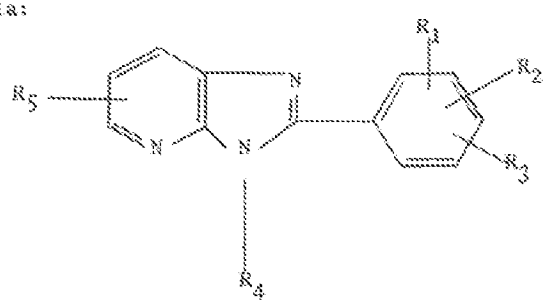
[A]

saccharine were dissolved in water and added. The solution was filtered pure.

[A]

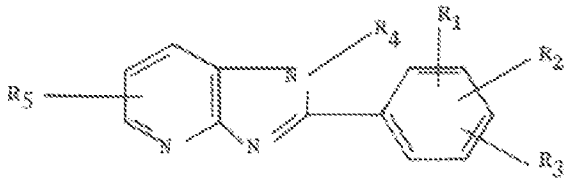
THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A process for the preparation of a compound of the general formula:



(I)

or an isomer thereof of the general formula:



(Ia)

wherein R_1 represents an alkylamino, dialkylamino, hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group, or an alkoxy group optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, 4-alkylpiperazino, 4-phenyl-piperazino, 4-methoxyphenylpiperazino, 4-phenylethylpiperazino, phenyl-ethylamino, N-methyl-phenylethylamino or N-methyl-dimethoxyphenylethyl-amino group;

R_2 represents a hydrogen or halogen atom or a hydroxy, methoxy, ethoxy, methyl, methylthio, methylsulfinyl or methylsulfonyl group;

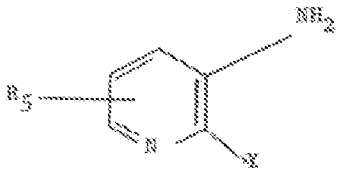
R_3 represents a hydrogen atom or a methoxy group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the remaining R_1, R_2 or R_3 group is as hereinbefore defined;

R_4 represents a hydrogen atom, an alkyl group optionally substituted by a hydroxy, phenyl, dimethoxyphenyl, dialkylamino, piperidino,

morpholino, 4-methylpiperazino or 4-phenylpiperazino group, or a phenyl group optionally substituted by a halogen atom or by one or two methoxy groups, whereby each of the above mentioned alkyl or alkoxy groups contain from 1 to 4 carbon atoms; and

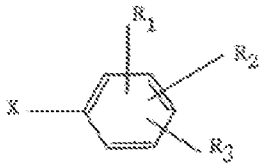
R_5 represents a hydrogen atom, a halogen atom or a lower alkyl group and the corresponding imidazo [4,5b] pyridine-N-oxides and isomers thereof and pharmaceutically acceptable acid addition salts thereof, which comprises either: -

(a) reacting a compound of the formula:



(II)

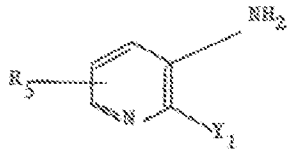
wherein R_5 is as hereinbefore defined and Y represents a group of the formula R_4NH-, wherein R_4 is as hereinbefore defined, with a compound of the formula



(III)

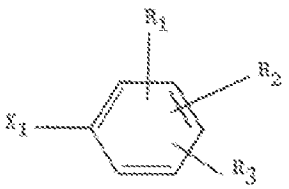
wherein R_1, R_2 and R_3 are as hereinbefore defined and X represents a carboxyl, thiocarboxyl or dithiocarboxyl group, or functional derivative thereof; or

(b) reacting a compound of the formula:



(IIa)

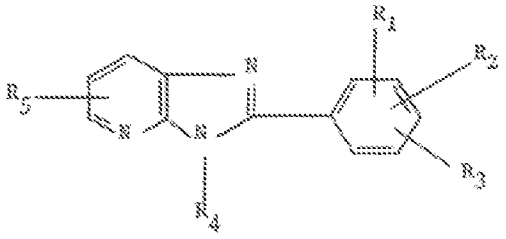
wherein R_5 is as hereinbefore defined and Y represents a halogen atom, with a compound of the formula:



(IIIa)

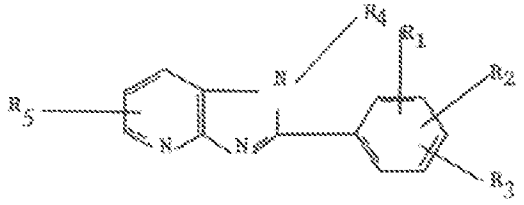
wherein R_1, R_2 and R_3 are as hereinbefore defined and X_1 represents an appropriate $-NR_4$ containing group which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group; and when a pharmaceutically acceptable acid addition salt is required converting a base of formula I obtained into such a salt.

2. A compound of the general formula:



(I)

or an isomer thereof of the general formula:



(Ia)

wherein R_1 represents an alkylamino, dialkylamino, hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group, or an alkoxy group optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, 4-alkylpiperazino, 4-phenylpiperazino, 4-methoxyphenylpiperazino, 4-phenylethylpiperazino, phenylethylamino, N-methyl-phenylethylamino or N-methyl-dimethoxyphenylethylamino group;

R_2 represents a hydrogen or halogen atom or a hydroxy, methoxy, ethoxy, methyl, methylthio, methylsulfinyl or methylsulfonyl group;

R_3 represents a hydrogen atom or a methoxy group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the remaining R_1, R_2 or R_3 group is as hereinbefore defined;

R_4 represents a hydrogen atom, an alkyl group optionally substituted by a hydroxy, phenyl, dimethoxyphenyl, dialkylamino, piperidino, morpholino, 4-methylpiperazino or 4-phenylpiperazino group, or a phenyl group optionally substituted by a halogen atom or by one or two methoxy groups, whereby each of the above mentioned alkyl or alkoxy groups contain from 1 to 4 carbon atoms; and

R_5 represents a hydrogen atom, a halogen atom or a lower alkyl group and the corresponding imidazo [4,5b] pyridine-N-oxides and isomers thereof and pharmaceutically acceptable acid addition salts thereof whenever prepared by the process of claim 1 or by an obvious chemical equivalent thereof.

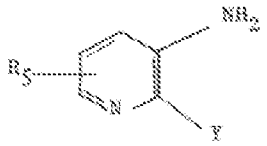
3. A process according to claim 1(a), in which the functional derivative is an acid halide, anhydride, ester or orthoester.

4. A process according to claim 1(b), in which $-NR_4$ is derived from a nitrile, amide, amidoester, imidothioester, imidohalide or amidine group.

5. A process according to claim 1, 3 or 4 in which R_4 represents a hydrogen atom.

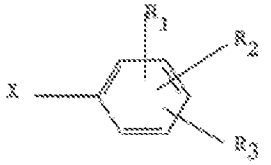
6. A process according to claim 1 in which R_4 and R_5 represent hydrogen atoms, R_2 represents a halogen atom or a methyl, methoxy, ethoxy, methylthio, methylsulfinyl, and R_3 represents a hydrogen atom or a methoxy group.

7. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 1 which comprises reacting a compound of formula



(II)

wherein R_5 and Y are as defined in claim 1 with a compound of formula

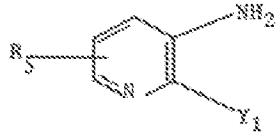


(III)

wherein R_1 to R_3 and X are as defined in claim 1 or a functional derivative thereof.

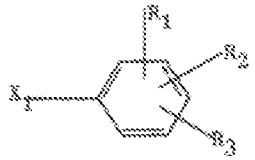
8. A process as claimed in claim 7 wherein the functional derivative is an acid halide, anhydride, ester or orthoester.

9. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 1 which comprises reacting a compound of formula



(IIa)

wherein R_5 and Y_1 are as defined in claim 1 with a compound of formula

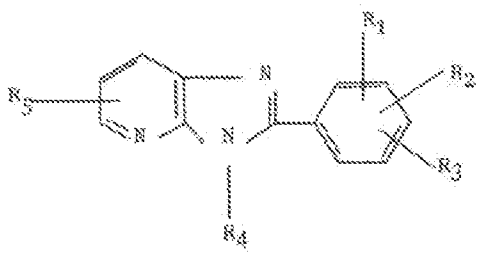


(IIIa)

wherein X_1 is as defined in claim 1 and wherein R_1 represents a hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group; an alkylamino or dialkylamino group, or an alkoxy group containing from 1 to 4 carbon atoms optionally substituted by a halogen atom or by a

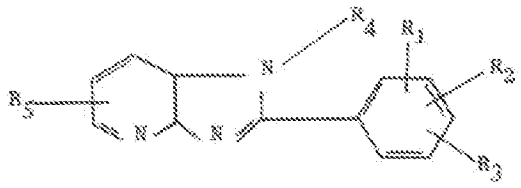
hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, N-methylpiperazino or N-phenylpiperazino group; R_2 represents a hydrogen or halogen atom; or a hydroxy, methoxy or ethoxy group; and R_3 represents a hydrogen atom or a methoxy group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the remaining R_1, R_2 or R_3 group is as defined above; each of the above mentioned alkyl groups containing from 1 to 4 carbon atoms .

10. A compound of the general formula:



(I)

or an isomer thereof of the general formula:



(Ia)

wherein R_1 represents a hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group; an alkylamino or dialkylamino group, or an alkoxy group containing from 1 to 4 carbon atoms optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, N-methylpiperazino or N-phenylpiperazino group; R_2 represents a hydrogen or halogen atom; or a hydroxy, methoxy or ethoxy group; and R_3 represents a hydrogen atom or a methoxy group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the remaining R_1, R_2 or

R_3 group is as defined above; each of the above mentioned alkyl groups containing from 1 to 4 carbon atoms; R_4 represents a hydrogen atom; and alkyl group optionally substituted by a hydroxyl, dialkylamino, phenyl or morpholino group, whereby each of the above mentionsd alkyl groups contains from 1 to 4 carbons; or a phenyl group optionally substituted by a halogen atom or a methoxy group; and R_5 represents a hydrogen or halogen atom or a lower alkyl group and physiologically compatible acid addition salts thereof, whenever prepared by the process of claim 9 or by an obvious chemical equivalent thereof.

11. A process as claimed in claim 9 wherein the said $-NR_4-$ containing group is a nitrile, amide, amido ester, imido thioester, imido halide or amidine group.

12. A process as claimed in any of claims 7, 8 or 9 wherein the reaction is effected in the presence of a solvent.

13. A process as claimed in any of claims 7, 8 or 9 wherein the reaction is effected at temperatures from -20 to 250°C.

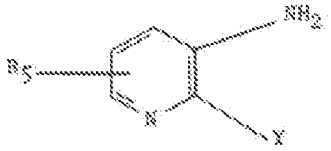
14. A process as claimed in either claim 7 or claim 9 wherein a compound of formula III or IIIa wherein X represents a carboxyl or an amide group is reacted with a compound of formula II or IIa as defined in claim 7 or claim 9 respectively in the presence of phosphorus oxychloride or thionyl chloride and in the presence of pyridine or triethylamine at temperatures from -20 to 120°C.

15. A process as claimed in claim 9 wherein a compound of formula IIIa wherein X represents a nitrile group is reacted with a compound of formula IIa as defined in claim 9 in the presence of a catalytic quantity of p-toluenesulfonic acid and at temperatures from 120 to 180°C.

16. A process as claimed in claim 9 wherein a compound of formula IIIa wherein X represents a thioamide group is reacted with a compound of formula IIa as defined in claim 9 at temperatures from 100 to 155°C.

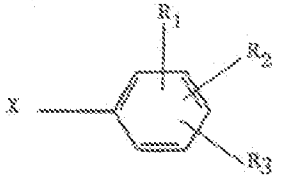
17. A process as claimed in claim 9 wherein a compound of formula IIa wherein Y represents a chlorine atom is reacted with a compound of formula IIIa as defined in claim 9 at temperatures from 100 to 200°C.

18. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 10 which comprises reacting a compound of formula



(II)

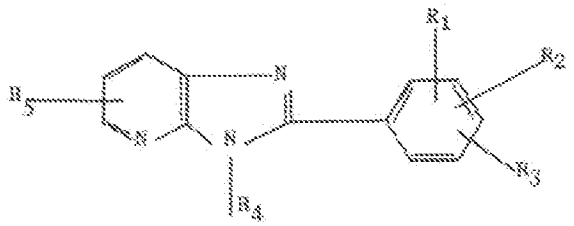
wherein R_5 is as defined in claim 10 and Y represents a group of formula R_4NH- wherein R_4 is as defined in claim 10 with a compound of formula



(III)

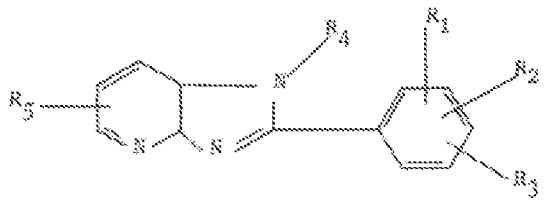
wherein R_1 to R_3 are as defined in claim 10 and X represents a carboxyl, thiocarboxyl or dithiocarboxyl group or with a functional derivative thereof.

19. A process for the preparation of a compound of the general formula:



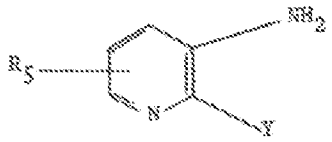
(I)

or an isomer thereof of the general formula:



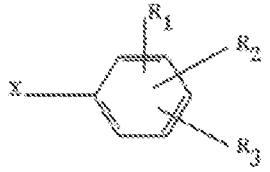
(Ia)

wherein R_1 represents a methyl-amino group, a morpholino group or piperazino group substituted in the 4-position by a phenyl group or by an alkyl group containing from 1 to 3 carbon atoms, or an alkoxy group containing from 2 to 4 carbon atoms substituted by a dimethylamino, diethylamino, piperidino, morpholino or thiomorpholino group, phenylethylamino, N-methylphenylethylamino or N-methyldimethoxyphenylethylamino group or by a piperazino group substituted in the 4-position by a methyl, phenyl, methoxyphenyl or phenylethyl group, R_2 represents a hydrogen, fluorine or chlorine atom, or a methoxy or ethoxy group; R_3 represents a hydrogen atom or a methoxy group; R_4 represents a hydrogen atom, an alkyl group containing from 2 to 4 carbon atoms substituted by a phenyl, dimethoxyphenyl, piperidino, morpholino, 4-methylpiperazino or 4-phenylpiperazino group; and R_5 represents a hydrogen atom and physiologically compatible acid addition salts thereof, which comprises reacting a compound of formula



(II)

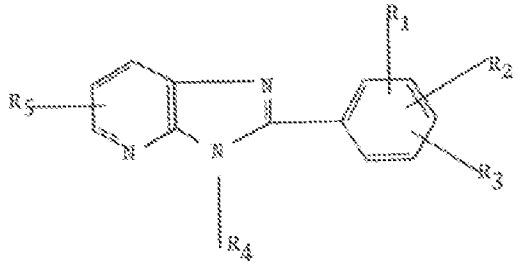
wherein R_5 represents a hydrogen atom and Y represents a group of formula R_4NH- (wherein R_4 is as defined above) with a compound of formula



(III)

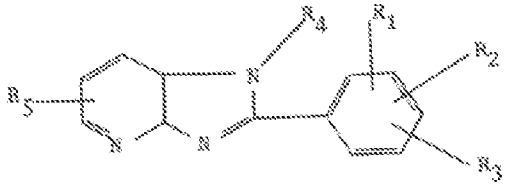
wherein R_1 to R_3 are as defined above and X represents a carboxy, thiocarboxy or dithiocarboxy group, or with a functional derivative thereof.

20. A compound of the general formula:



(I)

or an isomer thereof of the general formula:

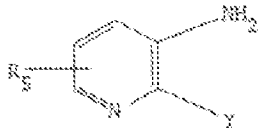


(Ia)

wherein R_1 represents a methyl-amino group, a morpholino group or piperazino group substituted in the 4-position by a phenyl group or by an alkyl group containing from 1 to 3 carbon atoms, or an alkoxy group containing from 2 to 4 carbon atoms substituted by a dimethylamino, diethylamino, piperidino, morpholino or thiomorpholino group, phenylethylamino, N-methylphenylethylamino or N-methyldimethoxyphenylethylamino group or by a piperazino group substituted in the 4-position by a methyl, phenyl, methoxyphenyl or phenylethyl group, R_2 represents a hydrogen, fluorine or chlorine atom, or a methoxy or ethoxy group; R_3 represents a hydrogen atom or a methoxy group; R_4 represents a hydrogen atom, an alkyl group containing from 2 to 4 carbon atoms substituted by a phenyl, dimethoxyphenyl, piperidino, morpholino, 4-methylpiperazino or 4-phenylpiperazino group; and R_5 represents a hydrogen atom and physiologically compatible acid addition salts

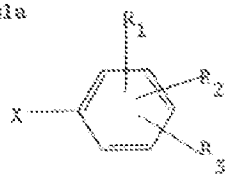
thereof whenever prepared by the process of claim 19 or by an obvious chemical equivalent thereof.

21. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 10 which comprises reacting a compound of formula



(II)

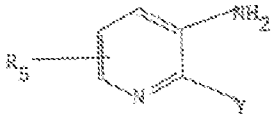
wherein R_5 is as defined in claim 10 and Y represents a halogen atom with a compound of formula



(III)

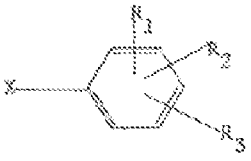
wherein R_1 to R_3 are as defined in claim 11 and X represents an appropriate $-NR_4-$ containing group (wherein R_4 is as defined in claim 10) which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group.

22. A process for the preparation of compounds of general formula I and isomers thereof of general formula Is as defined in claim 20 which comprises reacting a compound of formula



(II)

wherein R_5 represents a hydrogen atom and Y represents a halogen atom with a compound of formula



(III)

wherein R to R_3 are as defined in claim 20 and X represents an appropriate $-NR_4-$ containing group (wherein R_4 is as defined in claim 1) which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group.

23. A process as claimed in any of claims 1, 7 or 9 wherein a compound of formula I or Ia containing a reactive halogen atom thereby obtained is subsequently converted into the corresponding amino compound by reaction with an amine.

24. A process as claimed in any of claims 1, 7 or 9 wherein a compound of formula I or Ia containing a reacting hydrogen atom thereby obtained is subsequently alkylated by reaction with an alkylating agent in the presence of a base.

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25. A process as claimed in ~~any of~~ claim~~s~~ 1, ~~7 or 9~~ wherein a compound of formula I or Ia thereby obtained is subsequently converted into the corresponding N-oxide, S-oxide or S,S-dioxide compound by means of an oxidising agent.

26. A process according to claim 1 in which R_1 and R_2 are methoxy groups in the 2- and 4- positions and R_3, R_4 and R_5 are hydrogen atoms.

27. A process according to claim 1 in which 2-(2,4-dimethoxyphenyl)-1H-imidazo[4,5-b]pyridine or its hydrochloride are prepared by either:- (a) reacting 2,3-diaminopyridine with 2,4-dimethoxybenzoic acid in phosphorus oxychloride, thionyl chloride, pyridine; or (b) reacting 2,4-dimethoxylbenzoyl chloride with 2,3-diaminopyridine; (c) heating 2-amino-3-(2,4-dimethoxybenzoyl-amino) pyridine hydrochloride alone or in a solvent or reacting it with phosphorus oxychloride and pyridine; or (d) reacting methyl 2,4-dimethoxybenzoate with 2,3-diaminopyridine in phosphorus oxychloride; or (e) reacting 2,4-dimethoxybenzoylmorpholine with 2,3-diaminopyridine in pyridine containing phosphorus oxychloride, or (f) reacting 2,4-dimethoxylbenzoyl(4-chloroanilide) with 2,3-diaminopyridine in phosphorus oxychloride; or (g) reacting 2,4-dimethoxybenzoic acid-N-(4-chlorophenyl)-N^1-(2-amino-3-pyridyl)amidine hydro-

B

chloride; or (h) reacting 2,3-diaminopyridine with 2,4-dimethoxybenzonitrile and p-toluene sulfonic acid; or (i) reacting 2,3-diaminopyridine with 2,4-dimethoxybenzoyl morpholide and triethylamine; or (j) reacting 2,3-diaminopyridine with 2,4-dimethoxybenzoyl anhydride; or (k) reacting 2,4-dimethoxythiobenzoic acid-morphalide-methiodide with 2,3-diaminopyridine.

28. 2-(2,4-Dimethoxy-phenyl)-1H-imidazo[4,5-b]pyridine or its hydrochloride whenever prepared by the process of claim 27 or by an obvious chemical equivalent thereof.

29. A process according to claim 1 in which R_1 is 2-methoxy, R_2 is 4-methylmercapto and R_3, R_4 and R_5 are hydrogen atoms.

30. A process according to claim 1 in which 2-(2-methoxy-4-methylmercaptophenyl)-1H-imidazo[4,5-b] pyridine hydrochloride is prepared by reacting 2-methoxy-4-methylmercaptobenzoic acid morpholide with 2,3-diaminopyridine and phosphorus oxychloride.

31. 2-(2-Methoxy-4-methylmercapto-phenyl)-1H-imidazo-[4,5-b]pyridine hydrochloride whenever prepared by the process of claim 30 or by an obvious chemical equivalent thereof.

32. A process according to claim 1 in which R_1 is 2-methoxy, R_2 is 4-methylsulfinyl, R_3, R_4 and R_5 are hydrogen atoms.

33. A process according to claim 25 in which 2-(2-methoxy-4-methylsulfinylphenyl)-1H-imidazo[4,5-b] pyridine and its hydrochloride are prepared by oxidising 2-(2-methoxy-4-methylmercaptophenyl)-1H-imidazo-[4,5-b]pyridine and when the hydrochloride is required, reacting the base so obtained with hydrogen chloride.

34. A process according to claim 33 in which the oxidation is effected by reaction with 3-chloroperbenzoic acid.

35. 2-(2-Methoxy-4-methylsulfinyl-phenyl)-1H-imidazo[4,5-b]pyridine and

its hydrochloride whenever prepared by the process of claims 33 or 34 or by an obvious chemical equivalent thereof.

36. A process according to claim 1 in which R_1 is 2-methoxy, R_2 is 4-methyl and R_3, R_4 and R_5 are hydrogen atoms.

37. A process according to claim 1 in which 2-(2-methoxy-4-methylphenyl)-1H-imidazo[4,5-b]pyridine and its hydrochlorides are prepared by reacting 2-methoxy-4-methyl-thiobenzoic acid-morpholide and 2,3-diaminopyridine and when the hydrochloride is required reacting the base so obtained with hydrogen chloride.

38. 2-(2-Methoxy-4-methyl-phenyl)-1H-imidazo[4,5-b]pyridine and its hydrochloride whenever prepared by the process of claim 37 or by an obvious chemical equivalent thereof.

39. A process according to claim 1 in which R_1 is 2-methoxy, R_2 is 5-methylmercapto and R_3, R_4 and R_5 are hydrogen atoms.

40. A process according to claim 1 in which 2-(2-methoxy-5-methylmercaptophenyl)-1H-imidazo[4,5-b]pyridine and its hydrochloride are prepared by reacting 2-methoxy-5-methylmercaptobenzoic acid morpholide with 2,3-diaminopyridine in phosphorus oxychloride, pouring into water and neutralising with a base and when the hydrochloride is required reacting the base so obtained with hydrogen chloride.

41. 2-(2-Methoxy-5-methylmercapto-phenyl)-1H-imidazo[4,5-b]pyridine and its hydrochloride whenever prepared by the process of claim 40 or by an obvious chemical equivalent thereof.

42. A process according to claim 1 in which R_1 is 2-ethoxy, R_2 is methyl and R_3, R_4 and R_5 are hydrogen atoms.

43. A process according to claim 1 in which 2-(2-ethoxy-4-methylphenyl)-1H-imidazo[4,5-b]pyridine and its hydrochlorides are prepared by reacting

2-ethoxy-4-methylthiobenzoic acid-morpholide-methiodide with 2,3-diamino-pyridine and when the hydrochloride is required reacting the base so obtained with hydrogen chloride.

44. 2-(2-Ethoxy-4-methyl-phenyl)-1H-imidazo[4,5-b]pyridine and its hydrochloride whenever prepared by the process of claim 43 or by an obvious chemical equivalent thereof.

45. A process according to claim 1 in which R_1 is 2-ethoxy, R_2 is 4-ethylpiperazine-1-yl and R_3, R_4 and R_5 are hydrogen atoms.

46. A process according to claim 1 in which 2-[2-ethoxy-4-(4-ethyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]-pyridine and its dihydrochloride are prepared by reacting 2-[2-ethoxy-4-(4-ethyl-piperazin-1-yl)-phenyl]-1,3-dithiolanium iodide with 2,3-diamino~~piperazine~~ pyridine, and when the dihydrochloride is required converting the base so obtained with hydrogen chloride.

47. 2-[2-Ethoxy-4-(4-ethyl-piperazin-1-yl)-phenyl]-1H-imidazo[4,5-b]-pyridine and its dihydrochloride whenever prepared by the process of claim 46 or by an obvious chemical equivalent thereof.

SUBSTITUTE

REMPLACEMENT

SECTION is not Present

Cette Section est Absente